EDF submitted a Freedom of Information Act (FOIA) request to the Food and Drug Administration (FDA) in October 2017 seeking documents related to 31 Food Contact Substance Notifications that FDA approved for 19 unique per- and poly-fluorinated alkyl substances (PFAS) from six companies between 2002 and 2016. To minimize delays and the burden of FDA, EDF agreed in early 2018 to narrow the request to those documents generated by the agency. Those documents generally consist of evaluations of the: 1) chemistry and exposure; 2) toxicology; and 3) environmental impacts.

For each of the 31 FCNs below, we provide the portion of the notifier's application related to chemistry and FDA's staff review memo assessing the chemistry of the proposed use. The links for the FCN below go to FDA's Inventory of Effective Food Contact Substance (FCS) Notifications webpage where the agency describes the chemicals and its approved uses.

For more information, contact Tom Neltner at 202-572-3263 or tneltner@edf.org.

Index to PFAS Food Contact Substance Notifications	Eff. Date	Page of PDF
I. PFAS use as water and oil repellent in the manufacture of paper and paperboard.		
a. Archroma (successor to Clariant)		
i. FCN 1493	12/31/14	3 of 1028
b. Asahi Glass Company		
i. FCN 599	6/29/06	35 of 1028
ii. FCN 604	8/5/06	65 of 1028
iii. FCN 1186	9/21/12	102 of 1028
iv. FCN 1676	9/21/16	124 of 1028
c. Chemours (successor to DuPont)		
i. FCN 885	6/9/09	152 of 1028
ii. FCN 940	4/3/10	199 of 1028
iii. FCN 1027	6/12/11	222 of 1028
d. Daikin America		
i. FCN 820	7/31/08	244 of 1028
ii. FCN 827	9/9/08	285 of 1028
iii. FCN 888	7/18/09	306 of 1028
iv. FCN 933	12/30/09	328 of 1028
v. FCN 1044	2/16/11	532 of 1028
e. Solenis		
i. FCN 314	4/23/03	567 of 1028

ii. FCN 487	7/14/05	596 of 1028
iii. FCN 518:	10/20/05	625 of 1028
iv. FCN 542	12/25/05	653 of 1028
v. FCN 746	11/04/07	683 of 1028
vi. FCN 783:	3/6/08	715 of 1028
f. Solvay Specialty		
i. FCN 187	3/23/02	756 of 1028
ii. FCN 195	5/14/02	778 of 1028
iii. FCN 398	4/13/04	801 of 1028
iv. FCN 416	7/27/04	823 of 1028
v. FCN 538	11/19/05	847 of 1028
vi. FCN 962	5/11/10	876 of 1028
II. For use in repeat-use food-contact articles.		
a. Chemours (successor to DuPont)		
i. FCN 510	10/13/05	905 of 1028
ii. FCN 511:	10/13/05	920 of 1028
iii. FCN 539:	11/22/05	935 of 1028
iv. FCN 598:	4/29/06	965 of 1028
v. FCN 947:	4/30/10	980 of 1028
vi. FCN 948:	4/6/10	1008 of 1028

ARCHROMA FCN 1493

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Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-methyl-, 2-(dimethylamino)ethyl ester, polymer with 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, N-oxides, acetates

2. CAS Registry Number

1440528-04-0

3. Trade or Common Name

(b) (4)

4. Other Chemical Names *(IUPAC, etc.)*

N,N-dimethylaminoethyl methacrylate copolymer with tridecafluorohexylethyl methacrylate, N-oxide, acetate;
2-Dimethylaminoethyl methacrylate copolymer with 1H,1H,2H,2H-perfluorooctyl methacrylate, N-oxide, acetate; Copolymer of 2-(dimethylamino) ethyl methacrylate with 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate, N-oxide, acetate

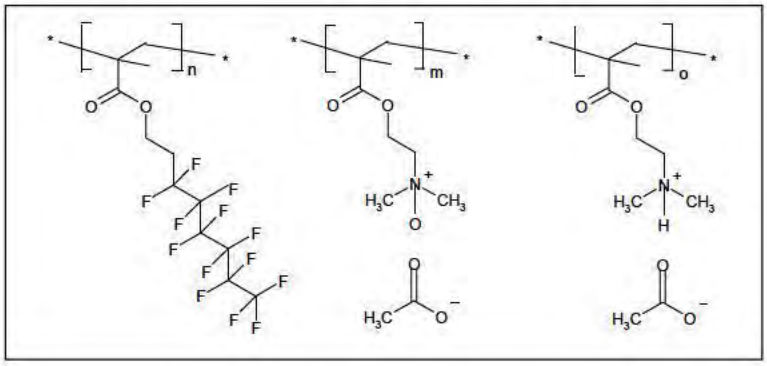
5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a copolymer produced from reaction of the following starting monomers, followed by partial oxidation of the dimethylaminoethyl methacrylate groups:

Chemical Name	CAS Reg. No.	Chemical Formula
2-Dimethylaminoethyl methacrylate	2867-47-2	$C_8H_{15}NO_2$
1H,1H,2H,2H-Perfluorooctyl methacrylate	2144-53-8	$C_{12}H_9F_{13}O_2$

The structure of the polymer may be represented as follows:



Representative samples of the polymer have been analyzed to determine the weight-average (M_w) and number-average (M_n) molecular weight. See **Attachment 1** for GPC report showing detailed results of the molecular weight determinations. Typical molecular weight values are as follows: (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)

The commercial product, (b) (4)(b) (4), is a liquid dispersion with the following typical composition:

CAS Reg. No.	Substance	Content, wt%
1440528-04-0	FCS Polymer	(b) (4)
(b) (4)		(b) (4)
		(b) (4)
		(b) (4)
		(b) (4)

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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

The FCS may be identified by its characteristic IR spectrum. See **Attachment 2.**

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?
1H,1H,2H,2H-Perfluorooctyl methacrylate	2144-53-8	Monomer	☒ Yes ☐ No
2-Dimethylaminoethyl methacrylate	2867-47-2	Monomer	☒ Yes ☐ No
(b) (4) [redacted]			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☒ Yes ☐ No

† If yes, include in Table II.B.3. If no, support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 3** for a description of the manufacturing process.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE *(continued)*

See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?
1H,1H,2H,2H-Perfluorooctyl methacrylate	2144-53-8	(b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4)		☒ Yes ☐ No
2-Dimethylaminoethyl methacrylate	2867-47-2			☒ Yes ☐ No
(b) (4)		281 ppm	< 1600 ppm	☒ Yes ☐ No
		163 ppm	< 300 ppm	☒ Yes ☐ No
		334 ppm	< 400 ppm	☒ Yes ☐ No
		< 27 ppm	< 1600 ppm	☒ Yes ☐ No
		Not detected (< 0.2 ppm)	Not detected (< 0.2 ppm)	☐ Yes ☒ No
		2.2 ppm	< 10 ppm	☒ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

Note: Impurity levels set forth above are reported on a "wet" formulated product (i.e., (b) (4)(b) (4) basis, which contains approximately (b) (4) FCS polymer solids. "Typical" residual concentrations above represent the average of concentrations measured in three representative FCS batches. "Maximum" residual concentrations are the maximum concentrations of the impurities anticipated by the Notifier.

(b) (4)

See **Attachment 4** for report of testing on representative FCS samples to determine the impurities identified above. Due to the high purity of the starting monomers, significant levels of other impurities will not be present. See **Attachment 5** for a report of testing conducted to characterize the monomers.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C - PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Consistency at 20°C (visual): Liquid	(b) (4)		
Solid content (IR-dryer for 30 minutes at 120°C)			
pH (measured as 5% solution in water)			
Viscosity at 20°C, mPa*s (Brookfield DV-I+, spindle 2, 100 rpm)			

Methods used to test for compliance with the specifications above may be found in **Attachment 6**.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C - PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

A report of GPC testing to determine the molecular weight distribution of representative FCS samples is provided in **Attachment 1**. Analyses were conducted using refractive index detection with poly(methyl methacrylate) calibration standards, and with dual detection with differential refractometer as concentration detector and multi-angle laser light scattering (MALLS) as molecular weight sensitive detector. The analyses were conducted on isolated polymer from three production batches.

Due to the fluorinated nature of the polymer, a molecular weight cut-off of 2000 daltons rather than 1000 daltons was used to determine the low molecular weight oligomer content. The higher threshold accounts for the comparatively high mass of the polymer relative to molecular size. The concentration of low molecular weight oligomers < 2000 daltons was below the limit of quantification (b) (4)

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SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☒ Repeat Use

The FCS is intended for use in the manufacture of paper and paperboard. The FCS will either be added to the pulp slurry at the wet-end of paper production or applied to the paper surface by size-press impregnation or coating. The finished paper and paperboard may be used in contact with all food types under FDA's Condition of Use B ("Boiling water sterilized") through H ("Frozen or refrigerated storage: Ready-prepared foods intended to be reheated in container at time of use").

The FCS will be used at a maximum level of 2.22 g of (b) (4)(b) (4) commercial liquid formulation per square meter of finished paper and paperboard. As indicated in Section A.5 above, the commercial formulation contains approximately 18% of polymer solids. Thus, the maximum use level corresponds to 0.26 mg polymer solids per square inch of paper and paperboard. (Calculated as follows: (2.22 g liquid/m^2 x 18% solids) x (1 m^2/1550 in^2) x (1000 mg/g) = 0.26 mg solids/in^2.)

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as not to preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS in this FCN, we have assumed that 10 grams of food will contact each square inch of surface area. In a repeated-use application, the amount of food contacted over the lifetime of the finished article would be far greater than 10 grams per square inch; thus, the exposure to the FCS estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

See **Attachment 7** for Suggested Regulatory Language.

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2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
For use in the manufacture of paper and paperboard, either added in the wet-end or applied to the paper surface, at levels up to 0.26 mg polymer solids per square inch of paper and paperboard surface area.	All food types (I-IX)	B, C, D, E, F, G, H

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS may be used under conditions that are subsumed by those described above for single-use articles.

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Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

The FCS is intended to impart oil and grease resistance to paper and paperboard. Oil and grease repellant properties are measured using the Kit Test (TAPPI Method 557). Typical values for these properties as a function of FCS application rate when applied at the size press are given in the following table.

Amount of FCS (g [redacted] liq /m^2)	Amount of FCS (mg polymer solids/in^2)	Kit Test Value
0.38	0.044	3
1.12	0.13	10
2.10	0.24	12

Note that increasing Kit values reflect increasing oil and grease repellance. Thus, the data demonstrate that the technical effect increases as the FCS addition level increases. The highest level tested is just below the maximum use level of 0.26 mg/in^2.

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SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

The report of a thermal stability study on the FCS is set forth in **Attachment 8**. Thermal analyses were conducted by differential scanning calorimetry (DSC) and by thermal gravimetric analysis (TGA). The analyses indicated a decomposition temperature of approximately 130°C. The maximum processing temperature is 100°C; thus, no degradation of the polymer is expected under the intended conditions of use.

Additional stability testing has been conducted to measure the generation of [redacted] upon heat treatment of the polymer. [redacted], [redacted] may be formed as a degradant by [redacted]. Thus, an increase in [redacted] content may be an indication of polymer degradation.

For this work, the FCS polymer was applied to paper sheets by size-press. [redacted] was measured by headspace GC-MS analysis after incubation of the treated paper samples for 30 minutes at 100°C. The samples were found to contain approximately [redacted]. These data suggest no decomposition of the polymer upon heating treated paper samples for 30 minutes at 100°C. See **Attachment 9** for report of the supplemental stability testing.

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Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
(b) (4) [redacted] The FCS polymer has been shown to be stable under the conditions of intended use, so no breakdown products are expected to be formed. However, as discussed previously, (b) (4) [redacted] Thus, (b) (4) [redacted] is a potential breakdown product of the FCS polymer. .	(b) (4) [redacted]		

STRUCTURE	STRUCTURE
(b) (4) [redacted]	

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

STRUCTURE	STRUCTURE

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SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II F 2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime (see Chemistry Recommendations, Appendix II, Part 4).

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D.3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration testing was conducted on paper sheets having a basis weight of 68 g/m^2 (0.044 g/in^2) that were treated at the size press with 6.5% (b) (4)(b) (4)(b) (4) and 8% of starch. The FCS batch used contained 18.3% of polymer solids, and the wet-product pick-up was 2.24 g/m . This corresponds to an FCS polymer solids content on the final paper of 0.41 g/m^2 (i.e., 2.24 g/m^2 x 18.3%), or 0.26 mg/in^2. The paper thickness was less than 0.05 cm and therefore only one side was considered in calculating migration.

Separate experiments were conducted to determine migration of (b) (4) a potential polymer decomposition product; the (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) and low molecular weight oligomers. The procedures used in each study are summarized below.

(b) (4) The treated paper sheets were cut into 12 squares of 1 in^2 each. The prepared samples were immersed in 120 mL of the food simulant.

(b) (4) To determine potential migration of (b) (4) the residual concentration in treated paper samples was determined by extraction with methanol. The coated paper samples (3.5 g) were cut into small pieces and immersed in 11 mL of methanol.

Low molecular weight oligomers: Due to the low concentration of oligomers in the FCS polymer and the absence of an oligomer standard, potential migration of FCS oligomers was determined with the use of (b) (4) (b) (4) (b) (4) . For this testing, the oligomer surrogate was added to the (b) (4) product (b) (4) The (b) (4) spiked product was applied to paper sheets at the size press as described above, to achieve an FCS polymer content of 0.26 mg/in^2. The treated paper sheets were cut into 16 squares of 1 in^2 each. The prepared samples were immersed in 160 mL of the food simulant.

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b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121 C/2 h, then 40 C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

(b) (4) To determine migration of (b) (4) test samples were exposed to 3% acetic acid, 10% ethanol, and olive oil. The testing was conducted under Condition of Use E (40°C for 10 days). The volume-to-surface-area ratio was 10 mL/in^2 and the coated paper surface area was 12 in^2. Analyses to determine (b) (4) in the extracts were performed after 24 hours, 48 hours, 96 hours, and 240 hours. Full details of the migration testing for (b) (4) under Condition of Use E are set forth in **Attachment 10**.

Subsequently, additional testing to determine migration of (b) (4) under Condition of Use B was conducted. For this purpose, FCS-treated paper samples were exposed to 10% ethanol and to olive oil for 2 hours at 100°C followed by 238 hours at 40°C. Analyses to determine (b) (4) in the extracts were performed after 2 hours, 24 hours, 96 hours, and 240 hours. Full details of the migration testing for (b) (4) under Condition of Use B are set forth in **Attachment 13**.

(b) (4) **:** To determine the residual concentration of the (b) (4) (b) (4) the test samples were extracted five times in succession with methanol at 60°C using an Accelerated Solvent Extractor (ASE). The individual extracts were collected for analysis, and the (b) (4) levels measured in each extract were summed to yield the total (b) (4) content. In each case (b) (4) was below the limit of detection by the fifth extraction, indicating that the successive extractions were exhaustive. The testing was performed in triplicate. Full details of the testing for residual (b) (4) are set forth in **Attachment 11.**

Low molecular weight oligomers: To determine migration of the low molecular weight oligomers, paper samples to which the (b) (4)(b) (4) FCS had been applied were exposed to 10% ethanol and olive oil. The testing was conducted under Condition of Use E (40°C for 10 days). The volume-to-surface-area ratio was 10 mL/in^2 and the coated paper surface area was 16 in^2. Analyses to determine the (b) (4)(b) (4) in the extracts were performed after 24 hours, 48 hours, 120 hours, and 240 hours. Full details of the migration testing on (b) (4)(b) (4)(b) (4) are set forth in **Attachment 12**.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4) (b) (4)	3% acetic acid	1 days at 40°C 2 days at 40°C 4 days at 40°C 10 days at 40°C	< 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2	< 129 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4) (b) (4)	10% ethanol	1 days at 40°C 2 days at 40°C 4 days at 40°C 10 days at 40°C	< 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2	< 129 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4) (b) (4)	Olive oil	1 days at 40°C 2 days at 40°C 4 days at 40°C 10 days at 40°C	< 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2 < 129 ng/in^2	< 129 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4)	Methanol	5 sequential extractions at 60°C using ASE	1.205 mg/kg 1.071 mg/kg 1.201 mg/kg	1.159 mg/kg in treated paper
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	Oligomer (b) (4)	10% ethanol	1 days at 40°C 2 days at 40°C 4 days at 40°C 10 days at 40°C	< 14 ng/in^2 < 14 ng/in^2 < 14 ng/in^2 < 14 ng/in^2	< 14 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	Oligomer (b) (4)	Olive oil	1 days at 40°C 2 days at 40°C 4 days at 40°C 10 days at 40°C	33 ng/in^2 42 ng/in^2 55 ng/in^2 66 ng/in^2	66 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4) (b) (4)	10% ethanol	2h/100°C 2h/100°C + 22h/40°C 2h/100°C + 94h/40°C 2h/100°C + 238h/40°C	< 133 ng/in^2 < 133 ng/in^2 < 133 ng/in^2 < 133 ng/in^2	< 133 ng/in^2
Paper treated at the size press with 0.26 mg/in^2 FCS polymer	(b) (4) (b) (4)	Olive oil	2h/100°C 2h/100°C + 22h/40°C 2h/100°C + 94h/40°C 2h/100°C + 238h/40°C	< 133 ng/in^2 < 133 ng/in^2 < 133 ng/in^2 < 133 ng/in^2	< 133 ng/in^2

Note: Due to space limitations, the values shown under the MIGRATION heading are the average of replicate measurements at each analysis interval. Individual replicate values may be found in the relevant reports attached. Where migrant levels varied over time, the value shown in the final column is the highest mean migration level found at any analysis interval.

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d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

The analyses for (b) (4)) (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4)) were validated in several ways, as described below.

(b) (4) Food simulants spiked with (b) (4) were subsequently exposed to the temperature/time conditions of the migration experiments both with and without treated paper test samples to check for stability under the test conditions. Additionally, extracts of treated paper samples were fortified at the end of the 10-day incubation to validate the extract analyses. The following table summarizes the validation testing on (b) (4) Full details of the validation procedure, results, and calculations are set forth in **Attachments 10 and 13**.

(b) (4) Validation – Condition of Use E				
Simulant	**Fortification/Incubation conditions**	**Spike Level (ppb)**	**Recovery (%)**	**RSD (%)**
10% ethanol in water	Spiked before 10 days at 40°C without paper	48.2	34.1	11.2
	Spiked before 10 days at 40°C with paper	49.6	60.6	25.7
	Paper extracts spiked after 10 days at 40°C	20.2	85.7	10.1
3% acetic acid in water	Spiked before 10 days at 40°C without paper	48.2	57.0	19.5
	Spiked before 10 days at 40°C with paper	49.6	46.5	16.2
	Paper extracts spiked after 10 days at 40°C	20.2	121.2	1.1
Olive oil	Spiked before 10 days at 40°C without paper	48.2	48.3	2.6
	Spiked before 10 days at 40°C with paper	49.6	51.8	0.6
	Paper extracts spiked after 10 days at 40°C	20.2	123.7	8.4

(b) (4) Validation – Condition of Use B				
Simulant	**Fortification/Incubation conditions**	**Spike Level (ppb)**	**Recovery (%)**	**RSD (%)**
10% ethanol in water	Spiked before 10 days at 40°C without paper	54.4	36.3	8.3
	Spiked before 10 days at 40°C with paper	54.4	48.9	1.7
	Paper extracts spiked after 10 days at 40°C	27.2	103.8	7.1
Olive oil	Spiked before 10 days at 40°C without paper	58.3	58.1	2.5
	Spiked before 10 days at 40°C with paper	58.3	78.2	0.8
	Paper extracts spiked after 10 days at 40°C	29.2	92.5	4.2

Oligomers: Food simulants spiked with the (b) (4)(b) (4) were subsequently exposed to the temperature/time conditions of the migration experiments without treated paper test samples to check for stability under the test conditions. Additionally, extracts of treated paper samples were fortified at the end of the 10-day incubation to validate the extract analyses. The following table summarizes the validation testing on the (b) (4)(b) (4) Full details of the validation procedure, results, and calculations are set forth in **Attachment 12**.

Simulant	**Fortification/Incubation conditions**	**Spike Level (ppb)**	**Recovery (%)**	**RSD (%)**
10% ethanol in water	Spiked before 10 days at 40°C without paper	7.57	94.6	2.2
	Paper extracts spiked after 10 days at 40°C	3.04	98.5	6.9
Olive oil	Spiked before 10 days at 40°C without paper	7.73	118.1	13.5
	Paper extracts spiked after 10 days at 40°C	3.86 7.73 15.45	132.1 108.6 109.3	1.9 5.7 22.9

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2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

[redacted] Migration of [redacted] was determined under both Conditions of Use E and B. [redacted] was below the limit of quantification in all cases. For the Condition of Use E testing, this corresponds to < 129 ng/in^2 in all food simulants. For the Condition of Use B testing, migration was < 133 ng/in^2.

We note that although the validation according to FDA procedures (i.e., extracts spiked after 10-day incubation) yielded acceptable recoveries, the recoveries were lower in the experiments where solvents were spiked before the 10-day exposure (with or without paper). This suggests that there could have been some loss of the analyte due to volatilization. For the sake of conservatism, we will estimate migration of [redacted] based on the quantification limit in the Condition of Use B testing (133 ng/in^2), corrected to reflect the lowest recoveries found in the stability/validation testing. For 10% ethanol extracts, the corrected LOQ = 133 ng/in^2 ÷ 36.3% = 366 ng/in^2. For olive oil extracts, the corrected LOQ = 133 ng/in^2 ÷ 58.1% = 229 ng/in^2. The corresponding concentrations in food are < 36.6 ppb in aqueous food and < 22.9 ppb in fatty food based on a ratio of 10 grams of food per square inch.

FCS Oligomers: Migration of FCS oligomers was evaluated with the use of [redacted] as discussed in Section F.1 above. [redacted] Thus, the data generated on migration of [redacted] from treated paper samples may be used to conservatively estimate FCS oligomer migration. As shown above, migration of [redacted] under Condition of Use E was below 14 ng/in^2 in 10% ethanol and averaged 66 ng/in^2 in corn oil after 10 days. These levels correspond to concentrations of < 1.4 ppb in aqueous food types and 6.6 ppb in fatty food types based on a ratio of 10 grams of food per square inch.

As discussed in Section F.1 above, the FCS-treated paper samples were cut in small pieces and immersed in the food simulants so that the samples were exposed on all sides. Under these severe conditions, the exposure to the food simulants at 40°C for 10 days is expected to result in an essentially exhaustive extraction. This expectation is supported by the results of the testing on [redacted] as migration was not higher under Condition of Use B than under Condition of Use E. Consequently, we respectfully submit that the existing migration data may be relied on as providing a valid estimate of oligomer migration under the full range of conditions of use proposed, i.e., Conditions of Use B through H.

DTBD: Worst-case migration of the [redacted] may be calculated based on the testing described in Attachment 11. As shown above, the average concentration of [redacted] in three paper samples treated with the FCS at the size-press was 1.159 mg/kg, or 1.159 µg/g of paper. Worst-case migration of [redacted] to food may be calculated based on the assumption that 100% of the [redacted] present in paper having a standard basis weight of 0.05 gram per square inch migrates to 10 grams of food per square inch. The calculation is as follows: (0.05 g paper/in^2 x 1.159 µg/g paper) ÷ 10 g food/in^2 = 0.0058 µg/g food, or 5.8 ppb.

Other impurities: The worst-case migration of all other potential impurities in the FCS may be calculated based on the concentrations present in the FCS as summarized in Section B.3 above and as reported in detail in **Attachment 4**. These calculations are set forth in **Attachment 14**.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations (*see Chemistry Recommendations Appendix IV*). If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq}) + (M_{ac})(f_{ac}) + (M\,al)(f_{al}) + (M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Dietary Exposure to [redacted] Dietary exposure to [redacted] is calculated based on the migration data summarized in Section F.1 above, adjusted as discussed in Section F.2 to reflect low recovery. The maximum migration levels are 36.6 ppb in 10% ethanol, which simulates aqueous, acidic, and alcoholic foods, and 22.9 ppb in olive oil, which simulates fatty food. Note these values are conservative, as migration was not detected above the LOQ.

Using these worst-case migration values, as well as the food-type distribution factors ($f_{aq} = 0.55$, $f_{ac} = 0.04$. $f_{al} = 0.01$, $f_{fat} = 0.40$) for polymer-coated paper and the consumption factor (0.05) for specialty coated paper, the DC and EDI are calculated as follows:

<M> = (36.6 ppb x 0.6) + (22.9 ppb x 0.4) = 31.1 ppb
DC = 31.1 ppb x 0.05 = 1.56 ppb, or 1.56 µg/kg food
EDI = 1.56 µg/kg food x 3 kg food/p/d = 4.67 µg/p/d

Dietary Exposure to FCS Oligomers: Dietary exposure to FCS oligomers is calculated based on the migration data summarized in Section F above. As discussed there, migration to 10% ethanol was <1.4 ppb; we will assume, conservatively, that oligomers will be present in aqueous, acidic, and alcoholic food at a level of 1.4 ppb. We will assume oligomers migrate to fatty food at a level of 6.6 ppb based on the data in olive oil. The calculations are as follows:

<M> = (1.4 ppb x 0.6) + (6.6 ppb x 0.4) = 3.48 ppb
DC = 3.48 ppb x 0.05 = 0.174 ppb, or 0.174 µg/kg food
EDI = 0.174 µg/kg food x 3 kg food/p/d = 0.52 µg/p/d

For the remaining potential impurities of the FCS, a single worst-case migration value is calculated based on measurements of residual levels in the FCS or in the treated paper. These calculations are set forth in Section F.2 above (b) (4) and **Attachment 14** (other impurities). For these substances, the weight-average migration is identical to the worst-case calculated migration value. Thus, the DC may be directly calculated by multiplying the worst-case migration value by the CF of 0.05. The results of these calculations are set forth in Section G.3 below.

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2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

The dietary exposure calculations set forth above subsume the use of the food contact substance in repeated-use applications.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*

See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Low molecular weight oligomers (<2000 daltons) of FCS	1440528-04-0	3.48 ppb	0.174 ppb	0.52 µg/p/d	0.174 ppb
(b) (4)	(b) (4)	31.1 ppb	1.56 ppb	4.67 µg/p/d	
1H,1H,2H,2H-Perfluorooctyl methacrylate	2144-53-8	43 ppb	2.15 ppb	6.45 µg/p/d	
2-Dimethylaminoethyl methacrylate	2867-47-2	7.9 ppb	0.40 ppb	1.2 µg/p/d	
(b) (4)		43 ppb	2.15 ppb	6.45 µg/p/d	
		5.8 ppb	0.29 ppb	0.87 µg/p/d	
		0.029 ppb	0.0015 ppb	0.0044 µg/p/d	
		1.4 ppb	0.070 ppb	0.21 µg/p/d	

NOTE: For all potential migrants other than oligomers, the calculations above are exaggerative as they either are based on limits of quantification for analytes (C6-EA) that were below the LOQ in migration testing, or are calculated based on the maximum anticipated residual concentrations in the polymer. The actual exposures to these substances are expected to be lower than the worst-case calculated levels.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: December 17, 2014

From: Division of Food Contact Notifications, HFS-275
Chemistry Review Team 1
LaShonda T. Cureton, Ph.D.

Subject: **FCN #0001493:** Keller and Heckman LLP (K&H), on behalf of Archroma Management GmbH (Archroma), for the use of a copolymer of 2-(dimethylamino)ethyl methacrylate with 3,3,4,4,5,5,6,6,7,7,8,8,8-trideacfluorooctyl methacrylate, N-oxide, acetate in the manufacture of food-contact paper and paperboard. Original Receipt: September 2, 2014; Deficiency Response Receipt: October 22, 2014.

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 2
Attn: Paul Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of Archroma Management GmbH (Archroma), submitted this Food Contact Notification (FCN) for the use of a copolymer of 2-(dimethylamino)-ethyl methacrylate with 3,3,4,4,5,5,6,6,7,7,8,8,8-trideacfluorooctyl methacrylate, *N*-oxide, acetate (b) (4)(b) (4)(b) (4)(b) (4) (CAS Reg. #1440528-04-0) added to the pulp slurry or the paper surface, at a maximum level of 0.26 mg/in^2 on a polymer solids basis, in the manufacture of food-contact paper and paperboard. Paper and board manufactured from the FCS may be used in contact with all food types under Conditions of Use B–H. The FCS is marketed by Archroma as a liquid dispersion containing (b) (4) -% solids (b) (4)(b) (4)(b) (4)

The Chemistry information is contained in Form 3480 and 13 Attachments as follows: 1 – Molecular Weight Distribution (MWD); 2 – Characterization; 3 – Manufacturing process; 4 – Quantification of Impurities; 5 – Residual Monomer Data; 6 – Analytical Methods and Specifications; 8 – Thermal Stability Analysis; 9 – Characterization of an Impurity; 10–13 – Migration Analysis; 14 – Worst-Case Migration Calculations for Impurities. A Deficiency Letter (dated 10/3/14) requested information for two areas of our chemistry review: 1) explanation of the degree of oxidation for the FCS, and 2) a discussion or additional analytical data to support the calculated exposure to LMWO as a result of the intended use.

The notifier provided a response (dated 10/22/14) containing a discussion on the degree of oxidation of the FCS, the analytical method and degree of oxidation content in Appendices 2 (*N*-oxide Specification and Method) and 3 (Revised Manufacturing process in the Degree of Oxidation). The notifier also provided additional information on low molecular weight oligomers (LMWOs) by calculating 100% migration to food. The notifier did not provide any additional migration studies. Their responses for both requests were adequate.

The FCS is not currently regulated in 21 CFR 170–199 nor is it the subject of any effective FCNs.

Identity (Form 3480, Section II.A, and Attachments 1–2, 6)

Information on the identity of the FCS is contained in Form 3480, Section II.A, and Attachments 1–2, 6.

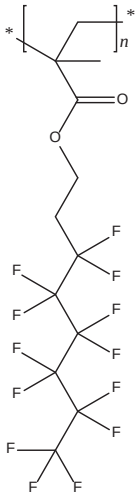
CAS Name: 2-Propenoic acid, 2-methyl-, 2-(dimethylamino)ethyl ester, polymer with 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, *N*-oxides, acetates

CAS Reg. #: 1440528-04-0

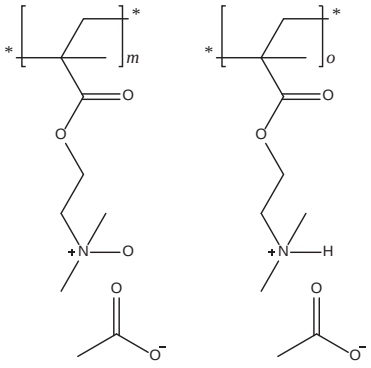
Trade Name: (b) (4)(b) (4)(b) (4)

Other Name: N,N-dimethylaminoethyl methacrylate copolymer with tridecafluorohexylethyl methacrylate, *N*-oxide, acetate; 2-Dimethylaminoethyl methacrylate copolymer with 1H,1H,2H,2H-perfluorooctyl methacrylate, *N*-oxide, acetate; Copolymer of 2-(dimethylamino) ethyl methacrylate with 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate, N-oxide, acetate

Structure: The FCS is a copolymer of 1H, 1H, 2H, 2H-perfluorooctyl methacrylate (CAS Reg. #2144-53-8) (aka (b) (4) structure 1) and of partially oxidized 2-(dimethylamino)ethyl methacrylate (DMAMET) (CAS Reg. #2867-47-2) (structures 2 and 3).



C6-MA



partially oxidized DMAMET

Commercial Product: The commercial product, (b) (4)(b) (4)(b) (4), consists of (b) (4) FCS dissolved in propylene glycol/water (see Table 1).

Table 1. Composition of Commercial Product

Substance	CAS Reg. #	Content, wt.-%
FCS	1440528-04-0	(b) (4)

Characterization

Gel permeation chromatography (GPC) (Attachment 1)

The notifier determined the molecular weight distribution (MWD) of three production batches of the FCS (Sample (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)) by GPC according to two methods as described in Attachment 1. In one method, a refractive index detector (RID) is which the MWD is determined *relative* to a poly(methyl methacrylate) standard calibration that conducted with known molecular weights of the poly(methyl methacrylate) standard. A second analysis used dual detection (a differential refractometer as a concentration detector and a multi-angle laser light scattering (MALLS), in which the MWD is determined without external calibration and *absolute* measurements are based on the change of the refractive index of a polymer solution relative to the change of the polymer concentration (d_n/d_c) and a molecules ability to scatter light at varying angles. The samples were measured in hexafluoroisopropanol (HFIP) solvent containing 5 mM sodium trifluoroacetate (NaTFA).

Average results of the number-average molecular weight (M_n) and weight-average molecular weight (M_w), and polydispersity (PDI) were listed on page 4 of Attachment 1 and are listed in Table 2, below.

Table 2. MWD for Three Batches of FCS

Batch	M_w	M_n	PDI	Fraction percentage (%), MW <2,000 Da
Poly(methyl methacrylate) Standard Calibration				
(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)	(b) (4)			<0.1 <0.1 <0.1
Dual Detection				
(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)	(b) (4)			<0.1 <0.1 <0.1

In Attachment 1, the notifier indicated that due to the fluorinated nature of the polymer, a molecular weight cut-off of 2,000 Da rather than 1,000 Da was used to determine the low molecular weight oligomer (LMWO) content. The higher threshold accounts for the comparatively high mass of the polymer relative to molecular size, thus, the LMWO content, <1,000 Da, was lower than the limit of

quantification of 0.1%.

FTIR Characterization (Attachment 2)

The spectrum of the FCS sample ([redacted]) was obtained on an FTIR PerkinElmer Spectrum One. The dried polymer was applied as it is using the so-called universal attenuated total reflectance (UATR) accessory. The notifier provided no correlation of the peaks to the polymer structure; however, the peaks are consisting with the monomers forming the polymer. A [redacted]

We have no questions regarding the identity and characterization of the FCS.

Manufacture (Form 3480, Section II.B, and Attachment 3)

Information on the manufacture of the FCS is contained in Form 3480, Section II.B, and Attachment 3. The manufacturing ingredients used to prepare the FCS are listed in Table 3, below.

Table 3. Manufacturing Reagents

Chemical Name	CAS Reg. #	Function	Use Level (wt.-%)
C6-MA	2144-53-8	Monomer	[redacted]
DMAMET	2867-47-2	Monomer	
[redacted]			

The manufacturing process of the FCS is conducted in [redacted] is summarized below:

Polymerization (Figure 1)

[redacted]

[redacted]

[redacted]

(b) (4)

Impurities (Form 3480, Section II.B.3, and Attachments 4–5)

Information on the impurities in the FCS is contained in Form 3480, Section II.B.3, and Attachments 4–5.

The notifier claimed that due to the high purity level of the monomers, C6-MA and DMAMET, several other impurities could be excluded. In Attachment 5, the purity of the monomers was analyzed by ^{1}H-, ^{13}C- and ^{19}F-nuclear magnetic resonance (NMR) spectroscopy and the characterization and maximum level of the impurities of the monomers were confirmed by GC. The (b) (4)

In Attachment 4, the residual content of different

gas chromatography-mass spectroscopy (GC-MS) and liquid chromatography-mass spectroscopy (LC-MS). The notifier reported residue levels of the impurities on a "wet-basis" in Attachment 4, Table 2, and summarized the typical and maximum values in Form 3480, which are included in Table 4, below.

Table 4. Impurity Profile [redacted]

Chemical Name	CAS Reg. #	Typical Residual (ppm)	Max. Residual (ppm)
C6-MA	2144-53-8	[redacted]	
DMAMET	2867-47-2		
[redacted]			

ND = not detected

[redacted]

We do not expect [redacted] to be present in the final food-contact material since it would volatilize during manufacturing and paper processing.

We have no questions regarding the manufacturing process and the impurity profile of the FCS.

<u>Physical/Chemical Properties (Form 3480, Section II.C and Attachment 6)</u>

Information on the physical/chemical properties of the FCS is contained in Form 3480, Section II.B, and the methods for analyzing the physical/chemical properties are included in Attachment 6 and are listed in Table 5, below.

Table 5. Physical/Chemical Properties

Physical/Chemical Properties	Maximum Value	Minimum Value	Individual Batch Values	Average of Batches
Consistency at 20°C (visual): Liquid	[redacted]			
Solid content (IR-dryer for 30 minutes at 120°C) (%)				
pH (measured as 5% solution in water)				
Viscosity at 20 °C, mPa*s (Brookfield DV-I+, spindle 2, 100 rpm)				

<u>Degree of Oxidation (Deficiency Response dated 10/22/14)</u>

In our Deficiency Letter (dated 10/3/14), we requested the notifier provide a specification on the minimum oxidation value for the FCS and a discussion or analytical information demonstrating that the samples utilized to determine migration consisted of the FCS at the minimum oxidation value (i.e., are worst case samples).

(b) (4)

Table 6. *N*-oxidation Results of three FCS Production Batches

Batch No.	*N*-oxide (%)
(b) (4)	

We have no questions regarding the physical/chemical properties of the FCS.

Intended Use and Technical Effect (Form 3480, Section II.D)

Information on the intended use and technical effect of the FCS is contained in Form 3480, Section II.D.

(b) (4) Paper manufactured from the FCS may be used in contact with all food types under Conditions of Use B–H, at a maximum level of 0.26 mg polymer solids/ in^2 of paper and paperboard. (b) (4) = 0.26 mg solids/in). The notifier has included use of the FCS in both repeat- and single-use applications.

The FCS is intended to impart oil and grease resistance to paper and paperboard. Oil and grease repellant properties are measured using the Kit Test (TAPPI Method 557). The notifier provides the typical values for these properties as a function of FCS application rate when applied at the size press are given in Table 7, below.

Table 7. Kit Test Values

Amount of FCS (g (b) (4) (b)	Amount of FCS (mg polymer solids/in^2)	Kit Test Value
0.38	0.044	3
1.12	0.13	10
2.10	0.24	12

The tables shows that the higher the amount of FCS, the higher the Kit value and the better the greaseproof property. We believe the data supports an incremental increase in the Kit Test Value at higher levels of the FCS.

We have no questions on the intended use and technical effect of the FCS.

Stability (Form 3480, Section II.E, and Attachment 8)

Information on the stability of the FCS is included in Form 3480, Section II.E, and Attachment 8.

In Attachment 8, the notifier provided the results of the thermal analyses by differential scanning calorimetry (DSC) and thermal gravimetric analysis (TGA). The thermograms indicate adequate stability of the FCS at temperatures higher than the use conditions (100 °C).

The notifier references Attachment 9 for stability testing, but we have described this study below under Migration to Food.

We have no questions on the stability of the FCS.

Migration to Food (Form 3480, Sections II.F, and Attachments 9–13)

Information on the migration and extraction experiments was contained in Form 3480, Section II.F, and Attachments 9–13. The studies are summarized in Table 8.

Table 8. Summary of Experimental Studies on Coated Paper

Attachment No.	Study type	Conditions	Analyte
9	Thermal	30 min at 100 ºC, followed by GC-MS analysis	(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)
10	Migration	Conditions of Use E	(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)
11	Extraction	Methanol using an Accelerated Solvent Extractor (ASE)	
12	Migration	Conditions of Use E	LMWO <2,000 Da
13	Migration	Conditions of Use B	(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)

Migration and Extraction Studies

For the studies in Attachments 10–13, the test samples consisted of paper sheets having a basis weight of 68 g/m^2 (0.044 g/in^2) that were treated at the size press with 6.5% FCS and 8% of starch. The FCS batch ((b) (4)(b) (4)(b) (4) used contained 18.3% of polymer solids, and the wet-product pick-up was 2.24 g/m . This corresponds to an FCS polymer solids content on the final paper of 0.41 g/m^2 (i.e., 2.24 g/m^2 * 18.3%), or 0.26 mg/in^2. The paper thickness was less than 0.05 g/in^2 and therefore only one side was considered in calculating migration. The notifier also notes in the Deficiency Response (dated 10/22/14) that data on the degree of oxidation of the sample used in the migration studies is not available.

The specific procedures used in each study are summarized below.

Determination of residual(b) (4) in coated paper (Attachment 9)

In Attachment 9, the notifier analyzed paper manufactured with the FCS to determine the level of [redacted] using headspace GC-MS. The test samples consisted of paper sheets having a basis weight of 68 g/m^2 (0.044 g/in^2) that were treated at the size press with 6.5% FCS and 8% of starch. The FCS batch [redacted] used contained 18.3% of polymer solids, and the wet-product pick-up was 2.24 g/m . Paper sheets were cut in small pieces. ~600 mg paper pieces were placed in a 20 mL headspace vial. The samples were fortified with 50 µL of the standard addition corresponding to a respective amount of [redacted] of 0.79 µg. The determination was performed in triplicate.

The samples were found to contain approximately 0.7 µg/dm^2 of [redacted] The theoretical content based on the pick-up of the liquid product (2.24 g/m^2) and the measured [redacted] concentration (315 mg/kg) in the FCS batch used to prepare the test samples, was 7 µg/dm^2 (Calculated as follows: 2.24 g/m^2 * 0.315 mg/g * 1 m^2/100 dm^2 * 1,000 µg/mg = 7 µg/dm^2).

Determination of [redacted] migration from coated paper with the FCS under Condition of Use E (Attachment 10)

The batch of FCS ([redacted] used for the paper application contained 315 mg/kg [redacted] The paper were cut into 12 square of 1 in^2 each and were immersed into 120 mL of food simulants, 10% ethanol, 3% acetic acid and olive oil, resulting in a surface area ratio of 10 mL/in^2.

The test specimen was incubated at 40 °C/240 h in the food simulants. The test solutions were sampled after 2, 24, 96 and 240 h in triplicate as defined by Condition of Use E. The test solutions were worked up and quantified via GC-MS.

As shown in Attachment 10, Table 2, the measured migration values were lower than the limit of quantification (LOQ) of 12.1 µg/kg. However, due to the low recovery rates in the different food simulants, the migration values were corrected.

Determination of residual [redacted] in coated paper (Attachment 11)

The residual content of [redacted] in paper treated with FCS was quantified by extraction and a worst case migration of [redacted] into food was calculated due to the higher level of [redacted] in the FCS.

The batch of FCS ([redacted] used for the paper application contained 366 mg/kg [redacted] The residual content of [redacted] in paper treated with FCS was determined by analysis of the test item after extraction with methanol using an Accelerated Solvent Extractor (ASE). The extracts were analyzed by GC-MS. The LOQ was 0.003 mg/kg paper. Each sample was extracted five times in succession.

As shown in Attachment 11 (Table 4), the average [redacted] found in extracts is 1.159 mg/kg (1.159 µg/g of paper). As shown in Table 5, the notifier calculated the worst-case migration assuming 100% migration of [redacted] to food (paper weight of 0.05 g/in^2 and 10 g of /in^2. The average result is calculated as follows: (0.05 g paper/in^2 * 1.159 µg/g paper) ÷ 10 g food/in^2 = 0.0058 µg/g food, or 5.8 ppb.

The notifier concludes that migration result could be due to the poor affinity of [redacted] for cellulosic fibers. Consequently, [redacted] is probably removed during the [redacted] process and will not migrate to food.

Determination of LMWO migration from coated paper (Attachment 12)

In order to estimate LMWO migration, the notifier determined the specific migration of an [redacted] from treated paper into 10% ethanol and olive oil under Condition of Use E. The batch of [redacted] used for application contained 0.054 w/w-% [redacted], corresponding to 0.3 wt.-% or the polymer content (0.054/0.18). (As noted above, GPC on the FCS indicated <0.1% LMWO <2,000 Da).

This batch of FCS (used for the paper application contained 0.054 w/w-% of the [redacted] (corresponding to 0.3 w/w-% of the polymer content). The surface area ratio was 10 mL/in and the coated paper surface area was 16 in^2. The paper samples were exposed to food simulants, 10% ethanol and olive oil.

The test specimen was incubated at 40 °C/240 h in the food simulants. The test solutions were sampled after 2, 24, 96 and 240 h in triplicate. The test solutions were worked up and quantified via GC-MS.

As shown in Attachment 12 (Tables 2–3), the measured migration values in 10% ethanol were lower than the LOQ 1.4 µg/kg. In olive oil, the highest average migration was 7.2 µg/kg was observed after an incubation of 240 h at 40 °C.

Determination of [redacted] migration from coated paper under Condition of Use B (Attachment 13)

This batch of FCS [redacted] used for the paper application contained 820 mg/kg [redacted] The paper were cut into 12 square of 1 in^2 each and were immersed into 120 mL of food simulants, 10% ethanol and olive oil, resulting in a surface area ratio of 10 mL/in^2.

The test specimen was incubated at 100 °C/2 h then 40 °C/240 h in the food simulants. The test solutions were sampled after 2, 24, 96 and 240 h in triplicate as defined by Condition of Use B. The test solutions were worked up and quantified via GC-MS.

As shown in Attachment 10 (Table 2), the measured migration values were lower than the LOQ of 13.6 µg/kg in 10% ethanol and 14.6 µg/kg in olive oil. However, due to the low recovery rates in the different food simulants, the migration values were corrected.

[redacted]

Summary of Migration Results

A summary of the average migration and extraction results from Attachments 9-13 are shown in Table 9, below.

Table 9. Summary of Results

Attachment No.	Migrant	Level	10% Ethanol (ng/in^2)	3% Acetic Acid (ng/in^2)	Olive Oil (ng/in^2)
9	(b) (4)	0.7 µg/dm^2			
10	(b) (4)(b) (4)		<129	<129	<129
11	(b) (4) (b) (4)	1.159 mg/kg in treated paper = 5.8 ppb			
12	LMWO (COU E)		<14		66
13	(b) (4)(b) (4)		<133		<133

Method Validation and Corrected (b) (4) Migration

Validation information for the migration analyses described in Attachments 10, 12–13 are summarized in Form 3480.

Food simulants spiked with (b) (4) were subsequently exposed to the temperature/time conditions of the migration experiments both with and without treated paper test samples to check for stability under the test conditions. Additionally, extracts of treated paper samples were fortified at the end of the 10-day incubation to validate the extract analyses. Full details of the validation procedure, results, and calculations are set forth in Attachments 10, 12–13.

We concur with the validation studies.

The notifier indicates that although the validation yielded acceptable recoveries, the recoveries were lower in the experiments where solvents were spiked before the 10-day exposure (with or without paper), which suggests that there could have been some loss of the analyte due to volatilization during the paper-making process. Thus, the notifier estimated migration of (b) (4) based on the quantification limit in the Condition of Use B testing (133 ng/in^2), corrected to reflect the lowest recoveries found in the stability/validation testing.

For 10% ethanol extracts, the corrected LOQ = 133 ng/in^2 ÷ 36.3% = 366 ng/in^2 **(<36.6 ppb)**
For olive oil extracts, the corrected LOQ = 133 ng/in^2 ÷ 58.1% = 229 ng/in^2 **(<22.9 ppb)**

Thus, these values would represent the corrected migrations for (b) (4)

Worst-Case Migration of the Impurities (Attachment 14)

In Attachment 14, the notifier provided worst-case migration estimates for the impurities using the residue values in Table 4 (above) and the assumption of 100% migration to food. Using (b) (4) as

an example:

<M> = (0.26 x 10^{-3} g FCS polymer/in^2 paper) x (1 g FCS formulation/0.18 g FCS polymer) x (<300 x 10^{-6} g residual (b) (4)(b) (4)(b) (4)(b) (4)) ÷ 10 g food/in^2 paper
= <4.3 x 10^{-8} g (b) (4) /g food
= <43 ppb (b) (4) in food

Using the calculation, the migration estimates for the impurities are listed in Table 10, below.

Table 10. Migration Values for Impurities

Chemical Name	CAS Reg. #	Max. Residual (ppm)	Migration (ppb)
C6-MA	2144-53-8	[redacted]	<43
DMAMET	2867-47-2		<8
(b) (4) [redacted]		<300	<43
		ND (<0.2 ppm)	<0.03
		<10	<1.4

Inspection of these Attachments indicates all contain an adequate amount of supporting data. We concur with the analysis and results and have no questions on the reported levels.

Revised LMWO Migration (Deficiency Response dated 10/22/14)

Our initial review indicates that the migration studies on the (b) (4)(b) (4)(b) (4) were only conducted under Condition of Use E, though FCN 1493 requested Conditions of Use B. In support of this extrapolation, the notifier states that these studies constitute "exhaustive extraction," and notes that migration testing for the impurity (b) (4) did not demonstrate increased migration under Condition of Use B (Attachment 13) when compared to Condition of Use E (Attachment 10). Indeed, the migration results for (b) (4) conducted under Condition of Use B and Conditions of Use E in 10% ethanol were both basically non-detect (<37.8 µg/kg compared to <19.8 µg/kg). Moreover, the (b) (4) (b) residue levels in the FCS formulation were different (b) (4) [redacted]

Nonetheless, in the Deficiency Letter (dated 10/3/14) we requested further discussion or additional analytical data to support the calculated exposure to LMWO as a result of the intended use of FCN 1493. The notifier in their Deficiency Response (dated 10/22/14) maintained that extraction of the (b) (4)(b) (4)(b) (4) at 40°C for 10 days is very severe for paper samples and is likely to result in essentially exhaustive extraction. As shown in Attachment 1, the LMWO content of the FCS was estimated to be below 0.1% based on GPC analysis. The FCS is proposed for use at a maximum level of 0.26 mg of polymer solids per square inch of treated paper and paperboard. Assuming FCS LMWO is present at 0.1% and that the finished paper contacts 10 g of food per square inch, the worst-case LMWO migration to food is calculated as follows:

0.26 mg/in^2 x <0.1% x 1 g/1000 mg ÷10 g food/in^2 = <2.6 x 10^{-8} g/g food, or <26 ppb.

We concur with the notifier approach to calculating migration of the FCS LMWO.

Exposure (Form 3480, Section II.G.3)

The notifier reported exposure estimates in Form 3480, Section II.G.3, based on the migration values from Attachments 10–14 and summarized in Tables 9 and 10, above.

The weight-average migration (<M>) was calculated by multiplying the migration to each food simulant (M_{FSL}), or the 100% migration value, by the sum of the food-type distribution factors (f_T) values for aqueous, acidic, and alcoholic foods (f_{aq} = 0.55, f_{ac} = 0.04, f_{al} = 0.01) or fatty foods (f_{fat} = 0.40). A consumption factor (CF) of 0.05 was used. This CF is appropriate for specialty-treated paper.

(b) (4) and LMWO

For (b) (4), the notifier used the migration information from Attachment 13 (10% ethanol, <36.6 ppb; olive oil <22.9 ppb). The results based on Attachments 9 and 13 were not used in our exposure estimates. Using (b) (4) as an example:

<M> = (<36.6 ppb x 0.6) + (<22.9 ppb x 0.4) = <31 ppb
DC = <31 ppb x 0.05 = <1.56 ppb, or <1.56 µg/kg food
EDI = <1.56 µg/kg food x 3 kg food/p/d = <4.67 µg/p/d

For LMWO, the notifier used migration values for 10% ethanol (<1.4 ppb) and olive oil (6.6 ppb) to calculate a DC of <0.17 ppb in a similar manner. However, using the revised LMWO migration of 26 ppb, we calculate a DC as follows:

DC = <26 ppb x 0.05 = <1.3 ppb or <1.4 µg/kg food
EDI = <1.3 µg/kg food x 3 kg food/p/d = <4 µg/p/d

Impurities (C6-MA, DMAMET, (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)

For the remaining impurities, the migration values in Table 10 were simply multiplied by the CF. The value for (b) (4) was taken from Table 9. The exposure estimates for results are summarized in Table 11, below.

Table 11. Exposure Estimates

Chemical Name	CAS Reg. #	Migration (ppb)	DC (ppb)	EDI (µg/p/d)
FCS LMWO	--	<26	<1.3	<4
(b) (4)	(b) (4)	<31	<1.6	<4.7
C6-MA	2144-53-8	<43	2.2	7
DMAMET	2867-47-2	<8	0.4	1
(b) (4)		<43	2.2	7
		<5.8	2.9	9
		<0.03	0.001	0.004
		<1.4	0.07	0.22

As this FCS is not currently regulated or the subject of an effective FCN, the exposure estimates for LMWOs may be considered cumulative exposures. We conclude the exposures for the impurities may be substitutional as there are other, similar FCSs that have similar impurities.

Notification Language

The notification language in the November 18, 2014 acknowledgement letter is adequate. We note that the letter specifically excludes use in contact with infant formula and breast milk.

Conclusion

We have no questions regarding the subject FCS.

Lashonda T. Cureton -S

Digitally signed by Lashonda T. Cureton -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001208683, cn=Lashonda T. Cureton -S
Date: 2014.12.17 09:52:05 -05'00'

LaShonda T. Cureton, Ph.D.

HFS-275 (R/F)
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Init: ABBailey: 12/16/14
Final: LTC: 12/17/14

ASAHI GLASS COMPANY FCN 599

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name 2-Propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester, polymer with 2-(diethylamino) ethyl 2-methyl propenoate, 2-hydroxyethyl-2-methyl-2-propenoate, and [redacted]

2. CAS Registry Number

863408-19-9

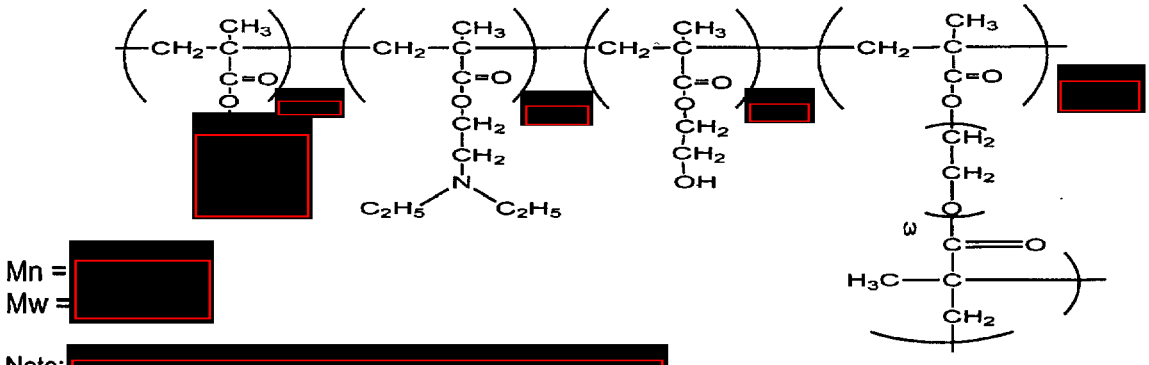
3. Trade or Common Name [redacted]

4. Other Chemical Names (IUPAC, etc.)

Copolymer of [redacted] 2-N,N-diethylaminoethylmethacrylate, 2-hydroxyethylmethacrylate,and 2,2'-ethylenedioxydiethyldimethacrylate

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



Mn = [redacted]
Mw =

Note: [redacted]

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

The IR spectrum may be found in Attachment 1.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
[redacted]		
2-N,N-diethylaminoethylmethacrylate	105-16-8	Monomer
2-hydroxyethylmethacrylate	868-77-9	Monomer
2,2'-ethylenedioxydiethyldimethacrylate	109-16-0	Monomer
[redacted]		
Acetic acid	64-19-7	Processing aid
Acetone	67-64-1	Processing aid
Water	7732-18-5	Solvent

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

The manufacturing process details and reaction stoichiometry are found in Attachment 2.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE - Continued

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (ppm)	Maximum Residual (ppm)
HEMA	868-77-9	178	
DEAM	105-16-8	137	

Ensure that exposures to these substances are addressed in Section II.G of this form.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value
N/A	

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches
Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications. **See Attachment 3 for supporting data.**

Property	Max. Value	Min. Value	Individual Batch Values
Appearance (visual)	[redacted]		
Solids (%)			
Specific Gravity (g/mL)			
pH			
Viscosity (mPa · s)			
Molecular Weight (10,000 D M_w)			

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

The maximum weight percentage of oligomers with MW < 2500 is 0.015%.

See Attachment 4 for analytical data.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

This product is a 20% aqueous dispersion of a fluorinated methacrylate (the FCS) in water and is intended for use on paper or paperboard in contact with all types of food (aqueous, acidic, alcoholic, and fatty) in a single use scenario under conditions of use B through H. Use of the dispersion in wet end processing of, or as a coating on, paper/paperboard will result in a maximum coating concentration of 1.2 wt % of the FCS in finished paper/paperboard.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
AG-UP1 is used in paper and paperboard (i) during wet-end manufacture at levels not exceeding 1.2% by weight, and/or (ii) as a coating not exceeding 1.2% by weight.	All food types: aqueous, acidic, alcoholic and fatty (types I through IX)	B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intend technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach da

The FCS is intended to impart oil, grease and water resistance to paper and paperboard. It may be added in the wet-end or at th press in cationic and non-ionic systems. **See Attachment 5.**

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure
None **See Thermogravimetric data in Attachment 6.**	N/A	N/A

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration test specimens were prepared with the FCS coated on bleached Kraft paper stock with a basis weight of 50 g/m^2 (32 mg/in^2). The paper was coated at the size press with a 12% aqueous solution of FCS (2.4 wt% polymer). The wet pick up was 53%. On drying, the actual polymer content on paper was 1.27%. Samples were extracted in immersion cells (96 in^2 in 385 mL solvent). Although the solvent to surface ratio was less than 10 ml/in^2, no evidence of solubility limited extraction was observed. Details of the sample preparation and extraction may be found in **Attachment 7.**

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Test and control articles were extracted in 10% ethanol and 95% ethanol at 100°C for 2 hours, followed by an additional 238 hours at 40°C (Condition of Use B). The extracts were sampled after 2, 24, 96 and 240 hours. Samples were extracted in immersion cells (96 in^2 in 385 mL solvent). Although the solvent to surface ratio was less than 10 ml/in^2, no evidence of solubility limited extraction was observed. Details of the extraction may be found in Attachment 7.

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
FCS Treated Paper	2-Hydroxyethyl methacrylate (HEMA)	10% Ethanol	100°C for 2 hr.	0.000142 mg/in² 0.000150 mg/in² 0.000151 mg/in²	0.000148 mg/in²
FCS Treated Paper	HEMA	10% Ethanol	100°C for 2 hr. then 40°C for 22 hr.	0.000140 mg/in² 0.000150 mg/in² 0.000148 mg/in²	0.000146 mg/in²
FCS Treated Paper	HEMA	10% Ethanol	100°C for 2 hr. then 40°C for 94 hr.	0.000147 mg/in² 0.000139 mg/in² 0.000144 mg/in²	0.000143 mg/in²
FCS Treated Paper	HEMA	10% Ethanol	100°C for 2 hr. then 40°C for 238 hr.	0.000147 mg/in² 0.000142 mg/in² 0.000145 mg/in²	0.000145 mg/in²
FCS Treated Paper	HEMA	95% Ethanol	100°C for 2 hr.	0.000146 mg/in² 0.000157 mg/in² 0.000168 mg/in²	0.000157 mg/in²
FCS Treated Paper	HEMA	95% Ethanol	100°C for 2 hr. then 40°C for 22 hr.	0.000156 mg/in² 0.000151 mg/in² 0.000153 mg/in²	0.000153 mg/in²
FCS Treated Paper	HEMA	95% Ethanol	100°C for 2 hr. then 40°C for 94 hr.	0.000141 mg/in² 0.000154 mg/in² 0.000156 mg/in²	0.000150 mg/in²
FCS Treated Paper	HEMA	95% Ethanol	100°C for 2 hr. then 40°C for 238 hr.	0.000150 mg/in² 0.000147 mg/in² 0.000152 mg/in²	0.000150 mg/in²

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
FCS Treated Paper	2-N,N-diethylaminoethylmethacrylate (DEAM)	10% Ethanol	100°C for 2 hr.	0.000158 mg/in² 0.000149 mg/in² 0.000148 mg/in²	0.000152 mg/in²
FCS Treated Paper	DEAM	10% Ethanol	100°C for 2 hr. then 40°C for 22 hr.	0.000203 mg/in² 0.000153 mg/in² 0.000155 mg/in²	0.000170 mg/in²
FCS Treated Paper	DEAM	10% Ethanol	100°C for 2 hr. then 40°C for 94 hr.	0.0000457 mg/in² 0.0000887 mg/in² 0.0000913 mg/in²	0.0000752 mg/in²
FCS Treated Paper	DEAM	10% Ethanol	100°C for 2 hr. then 40°C for 238 hr.	0.0000764 mg/in² 0.0000420 mg/in² 0.0000464 mg/in²	0.0000549 mg/in²
FCS Treated Paper	DEAM	95% Ethanol	100°C for 2 hr.	0.000404 mg/in² 0.000387 mg/in² 0.000394 mg/in²	0.000395 mg/in²
FCS Treated Paper	DEAM	95% Ethanol	100°C for 2 hr. then 40°C for 22 hr.	0.000326 mg/in² 0.000269 mg/in² 0.000257 mg/in²	0.000284 mg/in²
FCS Treated Paper	DEAM	95% Ethanol	100°C for 2 hr. then 40°C for 94 hr.	0.0000764 mg/in² 0.0000832 mg/in² 0.0000736 mg/in²	0.0000777 mg/in²
FCS Treated Paper	DEAM	95% Ethanol	100°C for 2 hr. then 40°C for 238 hr.	<0.0000100 <0.0000100 <0.0000100	<0.0000100

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

1. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

	Percent Recovery		
	10% Ethanol		
Analyte	LOD	Level 2	Level 3
2-Hydroxyethylmethacrylate (HEMA)	Detected	91.1	101
2-N,N-diethylaminoethylmethacrylate (DEAM)	Detected	77.0	88.3
	95% Ethanol		
2-Hydroxyethylmethacrylate (HEMA)	Detected	82.9	104
2-N,N-diethylaminoethylmethacrylate (DEAM)	Detected	87.0	115

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty.
See Attachment 8 for the EDI calculations.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

Memorandum

Date: May 31, 2006

From: Division of Food Contact Notifications
Chemistry Group I, HFS-275

Subject: FCN 599: AGC Chemicals Americas, Inc., through Pillsbury Winthrop Shaw Pittman, LLP, submissions of 12/30/05, 3/1/06, and 3/22/06. Perfluorinated grease-proofing agent based on C-6 chemistry for use on paper/paperboard.

To: Division of Food Contact Notifications
Regulatory Group II, HFS-275
Attn: P. Honigfort, Ph.D.

AGC Chemicals Americas, Inc. (AGC), through Pillsbury Winthrop Shaw Pittman LLC, has submitted a food contact notification (FCN) for use of the fluorinated copolymer produced by the polymerization of [redacted] 2-N,N-diethylaminoethyl methacrylate, 2-hydroxyethylmethacrylate, and 2,2'-ethylenedioxy diethyldimethacrylate (trade name [redacted]) to impart oil, grease, and water resistance to paper/paperboard, at a maximum use level of 1.2 wt-% of dry fiber, intended to contact all food types under conditions of use B through H. The food-contact substance (FCS) comprises 20 wt-% of the commercially marketed formulation, which is an aqueous dispersion trade named [redacted] The FCS is not currently authorized for any uses in or on food. The FCS was the subject of prenotification consultations [redacted] with AGC.

IDENTITY, MANUFACTURE, AND COMPOSITION

A. Identity

Chemical Name and CAS Registry No.

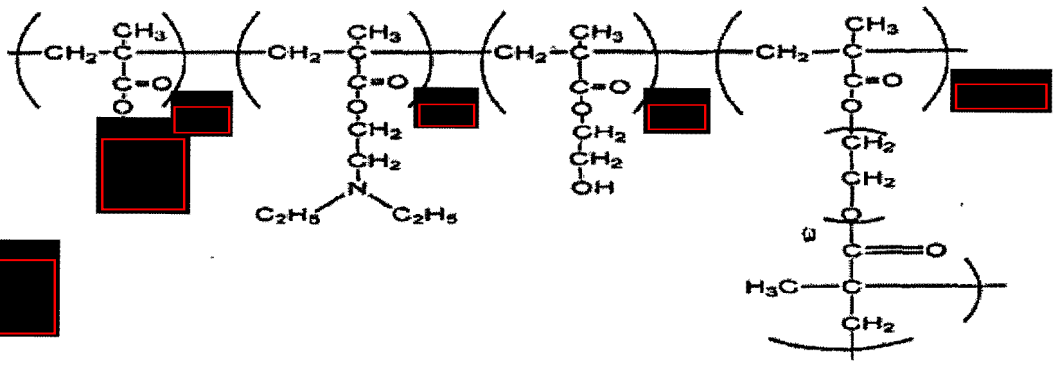
863408-19-9 — 2-propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester, polymer with 2-(diethylamino)ethyl 2-methyl propenoate, 2-hydroxyethyl-2-methyl-2-propenoate, and [redacted]

Common Names — copolymer of [redacted] 2-N,N-diethylaminoethylmethacrylate, 2-hydroxyethylmethacrylate, and 2,2'-ethylenedioxydiethyldimethacrylate

[redacted] (trade name for FCS)
[redacted] (developmental name for FCS)

[redacted] (trade name for aqueous dispersion)
[redacted] (developmental name for aqueous dispersion)

Structure



Mn = [redacted]
Mw = [redacted]

Ratios of monomer units are expressed in mole ratios.

The number average molecular weight (M_n) and weight average molecular weight (M_w) are typical values for the FCS as determined by size exclusion chromatography (SEC) with poly(methyl methacrylate) standards (see Attachment 4 to the FCN (FDA Vol. 7) for supporting data).

The notifier has demonstrated with the same SEC data that oligomers of molecular weight (MW) < 2500 comprise [redacted] of the FCS.

Physical Properties/Specifications (see Part II.C.2.a of Form 3480 and Attachment 3.A to the FCN (FDA Vol. 7))

Aqueous Dispersion	Appearance Percent solids Specific gravity (g/mL) pH Viscosity (mPa·s)	[redacted]
FCS	M_w (Daltons)	[redacted]

Data to Characterize the FCS

A Fourier transform IR spectrum of the dried FCS is given in Attachment 1 to the FCN (FDA Vol. 7).

The FCS is adequately identified.

B. Manufacture

The manufacturing process is adequately described in Attachment 2 to the FCN (FDA Vol. 7).

[redacted]

C. Composition

The notifier analyzed the finished aqueous dispersion of the FCS for 20 possible impurities, modeled the concentration of the polymerization initiator using the Arrhenius equation, and looked for [redacted] The analytical results for 18 of these impurities are given in Table 1 (see the detailed discussion below). A complete list of the impurities is given in Table 4. Two starting materials, acetone and acetic acid, are not included in the tables because 1) acetone [redacted] (i.e., exposure is essentially zero), and 2) acetic acid is affirmed as generally recognized as safe (GRAS) in 21 *CFR* 184.1005.

D. Stability

The thermal gravimetric and differential thermal analysis data provided in Attachment 6 to the FCN (FDA Vol. 7) indicate that the subject FCS is stable under the intended conditions of use.

[redacted]

INTENDED USE AND USE LEVEL

The FCS is intended to impart oil, grease, and water resistance to paper/paperboard intended to contact all food types under conditions of use B through H. The FCS may be added at the wet end or the size press during papermaking such that the total amount of the FCS in the finished paper/paperboard does not exceed 1.2 wt-% on a dry fiber basis. The FCS will be substitutional for other perfluorinated grease-proofing agents.

TECHNICAL EFFECT

The technical effect of the FCS in imparting oil, grease, and water resistance to paper/paperboard is adequately demonstrated in Attachments 5 and 7.A to the FCN (FDA Vol. 7). Results from the TAPPI "Kit" test and other measures of oil or water repellency consistently improved with increasing concentrations of the FCS applied to various paper samples at either the wet end or the size press.

TIERED APPROACH TO ESTIMATING EXPOSURE

A. Oligomers

The notifier calculated the concentration in food of low-molecular-weight oligomers (LMWO) of the FCS, assuming 100% migration to food and using the SEC data that demonstrated that oligomers of MW < 2500 comprise 0.015 wt-% of the FCS, the 1.2 wt-% use level of the FCS in paper, our average paper basis weight of 50 mg/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging (see Table 1):

$$\frac{0.00015 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.012 \text{ g FCS}}{\text{g paper}} \right| \frac{0.050 \text{ g paper}}{\text{in}^2} \left| \frac{\text{in}^2}{10 \text{ g food}} \right. = 9.0 \text{ µg/kg oligomers in food}$$

The notifier calculated the dietary concentration (DC) of the LMWO, using our recommended consumption factor (CF) of 0.05 for grease-proofed paper, and the estimated daily intake (EDI), assuming that individuals consume 3 kg of food per day. The results are summarized in Table 4. The calculations follow:

$$DC = (0.05 \text{ CF})(9.0 \times 10^{-9} \text{ g oligomers/g food}) = 0.45 \text{ ppb}$$

$$EDI = (0.45 \times 10^{-9} \text{ g oligomers/g food})(3000 \text{ g food/p/d}) = 1.4 \text{ µg/p/d}$$

Although the proposed use of the FCS is substitutional for the use of other perfluorinated grease-proofing agents, the LMWO in the subject FCS are different [redacted] of the other grease-proofing agents. However, use of the subject FCS will not result in an overall increase in exposure to perfluorinated oligomers of molecular weight ≤ 2500 Da.

B. Analysis of Aqueous Dispersion of FCS and 100% Migration Calculations

The notifier initially analyzed several production batches of the aqueous dispersion of the FCS for all possible impurities by solid phase microextraction gas chromatography with flame ionization detection (SPME/GC/FID), GC/FID, GC with mass spectrometric detection (MS), or high-performance liquid chromatography (HPLC). The results are given on p. 17 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1).

Raw data supporting these measurements are provided in Attachment 2 to the cover letter to the FCN (FDA Vol. 1) and in Attachments 3.G and 3.H to the FCN (FDA Vol. 7). However, we were unable to reproduce the results obtained by the notifier from the raw data provided. In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided sufficient raw data to enable us to complete the calculations for each of the impurities (see pp. 2-4 of the cover letter and Attachment 1 to the 3/1/06 submission).

Standard Addition Method

AGC used the standard addition method to determine the residual level of several of the impurities in the FCS. This involved spiking the aqueous dispersion of the FCS with increasing concentrations of the impurity of interest and constructing a standard addition curve of instrument response vs. spiked solution concentration. The y-intercept (x=0) of this standard addition curve is the instrument response to the unspiked sample, and the x-intercept (y=0) is the concentration of the unspiked sample.[1] If the concentration of the impurity of interest is determined in several industry batches, a new standard addition curve would normally be constructed for each sample because the x- and y-intercepts in each case are unique.

AGC used the standard addition curve determined for one lot of the aqueous dispersion of the FCS to calculate concentrations in several lots, arguing that the matrices of the samples were the same. AGC divided the peak area of each unspiked sample (the "y-intercept") by the slope of the standard addition curve to obtain the concentration of the impurity in each lot. As was stated above, a different standard addition curve should have been generated for each sample because the x- and y-intercepts will be different for each.

Based on the conservatisms built into our exposure estimates, we accept AGC's argument that the slope is the same for all the curves determined for each impurity. However, AGC's calculation does not account for the changes in the x- and y-intercepts or the data scatter that would result from experimentally determining the standard addition curve for each lot. We were able to account for these factors by moving each data point of the standard addition curve vertically by an amount equal to the difference in instrument response between the unspiked sample of interest and the unspiked sample used to construct the original standard addition curve. In this manner, we defined the correct line for each lot and determined the residual concentration of the impurity in each lot from the resulting x-intercept.

We found that AGC's simplified method for calculating the impurity concentrations could have resulted in underestimates of exposure by up to a factor of 20. In the case of ethylene glycol monoacetate (EGMAc), AGC obtained a concentration of 0.7 mg/kg in Lot 50251 of the aqueous dispersion of the FCS (see Attachment 2.G to the cover letter to the FCN (FDA Vol. 1)). With our more rigorous calculation, the result was 12 mg/kg (the x-intercept of our standard addition curve).[2] We therefore found it necessary to recalculate all the impurity concentrations that were based on the standard addition method. Our averaged results for four

[1] See http://zimmer.csufresno.edu/~davidz/Chem106/StdAddn/StdAddn.html for a more detailed explanation.

[2] This lot was not included in the final average value for EGMAc.

lots (14-2, 17-1, 17-2, and 50351) of each impurity are included in Table 1 (see Attachment 1 to the 3/1/06 submission for AGC's results).

Table 1. Residual Levels of FCS Components in the Aqueous Dispersion of the FCS and Concentrations in Food, Assuming 100% Migration (Corrected Results Are Indicated in Bold)

Substance	Analytical Method Calculation	Conc. in Aqueous Dispersion (mg/kg)	Conc. in Food (µg/kg)[a]
FCS oligomers of MW <2500	--	0.015 wt-% of dry FCS	9.0[b]
2-Diethylamino ethanol (DEAE)	Standard addition	**290.8**	**87.2**
Ethylene glycol (EG)	Standard addition	**36.3**	**10.9**
Diethylene glycol (DEG)	Calibration curve	< 31.5[c]	< 9.45
Ethylene glycol monoacetate (EGMAc)	Standard addition	**40.4**	**12.1**
Triethylene glycol (TEG)	Calibration curve	**35.9**	**10.8**
[redacted]			
Methacrylic acid (MAA)	Standard addition	**19.6**	**5.88**
Ethylene glycol dimethacrylate (EGDMA)	Standard addition	< 10.1[e]	< 3.03
[redacted]			
Triethylene glycol dimethacrylate (3ED or TEGDMA)	Calibration curve	**5.8**	**1.74**
Diethylene glycol monomethacrylate (DEGMMA)	Calibration curve	**3.4**	**1.02**
[redacted]			
Diethylene glycol dimethacrylate (DEGDMA)	Calibration curve	**< 0.89**[e]	**< 0.27**
[redacted]			
C8-C10 perfluorinated compounds	--	[redacted]	
[redacted]			

[a]Based on a use level of 1.2 wt-% FCS in finished paper, a concentration of 20 wt-% FCS in the aqueous dispersion, the average basis weight of food-contact paper of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging.

[b]Because SEC was conduced on the dry FCS, the 20 wt-% concentration of the FCS in the aqueous dispersion was not included in the calculation.

[redacted]

We note that AGC followed the standard addition method correctly in the analyses of [redacted] in that they generated standard addition curves for each sample and obtained the concentration from the x-intercept of each curve (see Attachments 2.V and 2.X to the cover letter to the FCN (FDA Vol. 2)).

Calibration Curve Method

AGC used a traditional calibration curve to convert peak areas to concentrations for the remaining impurities determined in the aqueous dispersion of the FCS. In each case, AGC forced the calibration curve through the origin and calculated the impurity concentrations by dividing the peak area of each sample by the slope of the calibration curve. We recalculated the correct linear functions, including y-intercepts, for these calibration curves and obtained much better statistical fits to the data than AGC did (see Attachment 1 to the 3/1/06 submission for AGC's results). Our averaged results for four lots (14-2, 17-1, 17-2, and 50351) of each impurity are included in Table 1.

It turned out that our calculated levels of the impurities in the aqueous dispersion of the FCS did not differ significantly from AGC's, with the exception of [redacted] which was twice that calculated by AGC. We found that the biggest changes occurred when the slope of the standard addition or calibration curve was high and/or the peak area for the sample was low. In many cases, the slope was very low and the peak area for the sample was relatively high. Also, averaging the results for the four production lots selected by AGC reduced the differences.

During our review of the raw data submitted in Attachment 1 to the 3/1/06 submission, we found that samples of the aqueous dispersion of the FCS had been diluted by 50% with methanol prior to analysis for six of the impurities (EGMAc, ethylene glycol, triethylene glycol, [redacted] methacrylic acid, and ethylene glycol dimethacrylate) without any indication that this dilution had been accounted for in the calculations. In the 3/22/06 response to your deficiency e-mail dated 3/8/06, the notifier provided a more detailed description of the analytical methods that demonstrated that the 50% dilutions had been accounted for. In the standard addition method, the spiking solutions were also diluted by 50%, and in the calibration curve method, the concentrations obtained from the calibration curve were doubled.

Polymerization Initiator and Its Breakdown Products

The notifier estimated the residual level of [redacted] polymerization initiator, in the aqueous dispersion of the FCS, using the Arrhenius equation to estimate decomposition (see p. 11 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1)). Three of the impurities listed in Tables 1 and 4 are decomposition products of the initiator: [redacted] which are discussed in a literature article [redacted] of the cover letter to the FCN (FDA

Vol. 2).[3] These were the major degradation products detected in an electron spin resonance (ESR) study of the initiator and comprised a total mass balance of 92 to 95% of the starting initiator in the following amounts: [redacted]

In analyses of the aqueous dispersion of the FCS, [redacted] were detected, while the [redacted] was not (exposure to [redacted] was later refined in a dichloromethane extraction study – see below). The fact that the [redacted] which contributed significantly to the mass balance of decomposition products, was [redacted] is strong evidence that the initiator [redacted] We have therefore concluded that the Arrhenius equation does not need to be used to establish an upper limit to the concentration of the initiator in the FCS and [redacted]

A fourth potential degradation product of the initiator, [redacted] which was listed as an impurity in [redacted] was not detected in the ESR study described in the literature article. The notifier stated in Attachment 2.R to the cover letter to the FCN (FDA Vol. 2) that the experimental conditions described in the literature article were "much more favorable to its generation" than the AGC polymerization reaction. We therefore agree with AGC that exposure to this substance is essentially zero.

Exposure Estimates

The notifier calculated the concentration in food of 15 of the 20 impurities determined by the above methods, assuming 100% migration of components of the FCS to food. The results are given in Table 1 (our corrected results are indicated in bold). The following is an example calculation for EGMAc, using its concentration in the aqueous dispersion of the FCS of [redacted] mg/kg (from Table 1), the 20 wt-% concentration of FCS in the aqueous dispersion, the 1.2 wt-% use level of the FCS in paper, our average paper basis weight of 50 mg/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging:

[redacted] $\frac{\text{1 g aq. dispersion}}{\text{0.20 g FCS}} \times \frac{\text{0.012 g FCS}}{\text{g paper}} \times \frac{\text{0.050 g paper}}{\text{in}^2\text{ paper}} \times \frac{\text{in}^2}{\text{10 g food}} =$ [redacted]

The DCs and EDIs for these impurities were calculated as described above for the oligomers (CF = 0.05). The results are given in Table 4 (our corrected values are indicated in bold). These values are conservative because they are based on measured levels of the impurities in the aqueous dispersion of the FCS and the assumptions that the impurities are completely retained throughout the papermaking process (which is highly exaggerative for cases in which the FCS is added at the wet end) and that they migrate 100% from paper to food.

[redacted]

C. Extraction of FCS-Coated Paper with Dichloromethane and 100% Migration Calculations

For the 6 impurities whose exposures as calculated above exceeded levels supported by the available toxicological data (plus [redacted] – at our request as a result of [redacted], the notifier extracted paper treated with the FCS into dichloromethane (DCM) under reflux conditions for 7 hr and then 16 hr and analyzed the extract for the impurities by GC/FID, GC/MS, or LC/MS. The results are given on pp. 18-19 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1), and the supporting raw data are given in Attachment 1.B (FDA Vol. 1).

In [redacted] we explained to AGC that DCM was not an appropriate solvent for total extraction of highly polar molecules [redacted] We also explained that the validation of the total extraction experiments, which consisted only of spike-and-recovery tests on the extracts, was not complete because it did not demonstrate that all of the impurity of interest was extracted from the paper. However, we agreed with AGC that, at a minimum, it is necessary to demonstrate that the extraction yielded results greater than or equal to those that would be obtained with a migration test conducted under the appropriate conditions for the intended use. AGC conducted appropriate migration tests on [redacted] The DCM extraction results are therefore validated.

Upon inspection of the raw data for the DCM extractions, we found that the sets of chromatograms given for [redacted] and [redacted] on pp. 112-118 and 120-125 of Attachment 1.B to the cover letter to the FCN (FDA Vol. 1) are identical, with [redacted] identified as the analyte peak on each of the chromatograms. In addition, the set on which [redacted] is labeled indicates that [redacted] was detected in both the 7- and 16-hr extracts of the paper sample treated with the FCS (see Figures 58 and 59 on pp. 123-124 of Attachment 1.B), while the final report indicates that [redacted] was not detected in these extracts (see p. 62 of Attachment 1.B). In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided the correct chromatograms for [redacted] and explained that [redacted] was detected in the extracts but below the limit of quantification (LOQ) of the analytical method (see pp. 4-5 of the cover letter and Attachment 4 to the 3/1/06 submission). We are satisfied with these data.

Exposure Estimates

The notifier calculated the concentration in food of 3 of the 6 impurities (plus [redacted] determined in this manner, assuming 100% migration of components of the FCS to food. The results are given in Table 2. We note that the basis weight of the paper used in the extraction studies was 32.26 mg/in^2. Because the FCS is added as a wt-% of the paper, higher migration would be expected per square inch of paper of a typical basis weight of 50 mg/in^2. The notifier therefore scaled up the concentrations in food by a factor of 1.55 (50 mg/in^2 / 32.26 mg/in^2 = 1.55) to account for this difference (see p. 15 of Attachment 1.A to the cover letter to

the FCN (FDA Vol. 1)). The DCs and EDIs for these impurities were calculated as described above. The results are given in Table 4.

Table 2. Results of Dichloromethane (DCM) Extraction of Paper Samples Coated with the FCS, Assuming 100% Migration of Impurities to Food

Substance	Conc. in DCM (μg/in^2)	Conc. in Food (μg/kg)[a]
[redacted]		

[a]Assuming that 10 g of food contact 1 in^2 of packaging. A factor of 1.55 was also applied to account for the low basis weight of the paper samples used in the extraction tests.
[b]Detected but below the LOQ of the analytical method.

These exposures were based on the LOQ of the analytical method used to determine the impurities. In each case, the impurity was detected but at a level below the LOQ. Unfortunately, a true limit of detection (LOD) was not established for the analytical method, so we cannot quantify a lower limit for the exposures. However, we can state that the exposures are less than those based on the LOQ.

D. Migration Testing (Part II.F.1 of Form 3480 and Attachment 7 to the FCN (FDA Vol. 7)

The remaining 3 impurities were determined via migration tests in which paper samples coated at the size press to contain 1.27 wt-% FCS (on a dry fiber basis) were immersed in 10% or 95% ethanol for 2 hr at 100° C, followed by 10 d at 40° C. The food simulants were then analyzed for the impurities by GC/MS. The results are given on pp. 1570-1571 of Attachment 7.B to the FCN (FDA Vol. 7).

We identified the following deficiencies in the raw data supporting the migration study:

1) In Table 9 of the spike-and-recovery validation data for 2-N,N-diethylaminoethylmethacrylate (DEAM) in 10% ethanol on p. 1586 of Attachment 7.B to the FCN, the "composite" or unspiked migration sample was reported to have an average DEAM concentration of 0.0403 μg/mL, and this value was subtracted from the measured concentrations of the spiked samples. The supporting chromatogram for the composite sample on p. 1620 of Attachment 7.B indicates that DEAM (ion 86) had a peak area of 9738 units, which is far below the 90,000 units shown to represent the LOQ of the method of 0.05 μg/mL for DEAM on the calibration curve shown on p. 1607 of Attachment 7.B. If no subtraction is made from the validation measurements, the percent recoveries become as high as 490%.

2) In Table 11 of the spike-and-recovery validation data for [redacted] in 95% ethanol on p. 1588 of Attachment 7.B to the FCN, values are reported for a "Level 4" spike. No supporting chromatogram was provided for this Level 4 spike. A chromatogram was provided for a "Level 3" spike on p. 1640 of Attachment 7.B. However, the peak area for [redacted] on this chromatogram was [redacted], which is comparable to the [redacted] shown to represent the LOQ of the method of [redacted] on the calibration curve shown on p. 1624 of Attachment 7.B. In addition, the [redacted] peak area is less than the [redacted] peak area given for the [redacted] "LOD spike" on p. 1638 of Attachment 7.B.

In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided adequate responses to these deficiencies (see pp. 5-7 of the cover letter to the 3/1/06 submission). In the case of deficiency 1, the notifier explained that they had provided an "example" calibration curve that did not correspond exactly to the samples that were analyzed. The notifier provided the correct calibration curve for the samples in Attachment 5 to the 3/1/06 submission. In the case of deficiency 2, the notifier provided the correct chromatogram for the "Level 4" spike in Attachment 6 to the 3/1/06 submission and explained that "Level 3" data were not developed for [redacted] due to a sample work-up issue. We are satisfied with the raw data, chromatograms, calibration curves, and calculations supporting the migration studies.

The migration tests were adequately validated by spike-and-recovery analysis at the LOQ of the analytical method and at two spiking levels above the LOQ. The recoveries of the three impurities ranged from [redacted]

Exposure Estimates

The concentrations in food of the three remaining impurities are given in Table 3, and the exposures are given in Table 4. The following is an example calculation of the DC of [redacted] using the concentrations in food given in Table 3, the food-type distribution factors (f_T) for polymer-coated paper, the CF of 0.05 for grease-proofed paper, and the 1.55 scale-up factor to account for the low basis weight of the paper samples used in the migration study (see above):

DC[redacted] = (0.05 CF)(1.55 scale-up factor)[redacted]
= [redacted]

EDI[redacted] = [redacted] (3000 g food/p/d) = [redacted]

E. Other Potential Impurities

At our request in [redacted] the notifier analyzed the aqueous dispersion of the FCS or DCM extracts of paper treated with the FCS for [redacted] C8-C10 perfluorinated compounds, and [redacted] The concentrations in food of these substances, assuming 100% migration, are given in Tables 1 and 2. The exposures are summarized in Table 4.

Table 3. Highest Results of Migration Studies Conducted on Paper Samples Coated with the FCS into 10% and 95% Ethanol for 2 hr at 100° C, Followed by 10 d at 40° C

Substance	Conc. in Food Simulant ($\mu g/in^2$)		Conc. in Food ($\mu g/kg$)[a]
[redacted]			
2-hydroxyethylmethacrylate (HEMA)	10% EtOH	0.148	14.8
	95% EtOH	0.157	15.7
2-N,N-diethylaminoethyl-methacrylate (DEAM)	10% EtOH	0.170	17.0
	95% EtOH	0.395	39.5

[a]Assuming that 10 g of food contact 1 in^2 of packaging. A factor of 1.55 was applied to <M> to account for the low basis weight of the paper samples used in the migration tests.
[b]Detected but below the LOQ of the analytical method.

[redacted] was determined in the aqueous dispersion of the FCS by HPLC/MS with an LOD of 0.03 µg/mL in the dispersion and an LOQ of 0.1 µg/mL (see Attachment 2.V to the cover letter to the FCN (FDA Vol. 2)) and in the DCM extracts by LC/MS with an LOQ of 0.01 $\mu g/in^2$ paper that was established by Covance (see pp. 99-110 of Attachment 1.B to the cover letter to the FCN (FDA Vol. 1)). [redacted] was detected in the aqueous dispersion of the FCS at an extremely low level between the LOD and the LOQ. [redacted] was not detected at all in the DCM extracts, i.e., no peak was discernable from the background noise.

We conclude that exposure to [redacted] is essentially zero for the following reasons: 1) [redacted] was not detected in the DCM extracts, which provide a more realistic estimate of migration to food than measurements in the aqueous dispersion of the FCS, 2) an exposure estimate based on the very high LOQ established for the DCM extraction study would be artificially high, especially considering that the notifier also applied a correction factor to account for the low basis weight of the paper samples used in the study, and 3) an exposure estimate based on the extremely low level measured in the aqueous dispersion of the FCS and a 100% migration calculation would be two orders of magnitude below that estimated from the LOQ of the DCM extraction study.

A range of C8-C10 perfluorinated compounds, excluding the acids, was determined in the FCS by GC/MS (see Attachment 2.W to the cover letter to the FCN (FDA Vol. 2)). [redacted]

[redacted] was determined in the aqueous dispersion of the FCS by HPLC/MS/MS with an LOQ of [redacted] in the dispersion (see Attachment 2.X to the cover letter to the FCN (FDA Vol. 2)). [redacted] was detected at an extremely low level of 1.2 ng/mL in the dispersion (the higher of two production batches), which is below the LOQ. Since no other data were provided to demonstrate that [redacted] was not expected to migrate to food (e.g., DCM extraction data for paper samples treated with the FCS), we have estimated exposure to PFOA to be [redacted] assuming 100% migration of the 1.2 µg/kg determined in the aqueous dispersion of the FCS.

Table 4. Exposures to All Components of the FCS (Corrected Results Indicated in Bold)

Substance	CAS Reg. No.	Function	Exposure Estimation Method	DC (ppb)	EDI (µg/p/d)
FCS oligomers of MW <2500	--	--	SEC msmt., 100% migration calc.	0.45[a]	1.4[a]
[redacted]					
2-diethylamino ethanol (DEAE)	100-37-8	Impurity in DEAM	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**4.4**	13
[redacted]					
2-hydroxyethylmethacrylate (HEMA)	868-77-9	Monomer	Migration study	1.2[c]	3.5[c]
2-N,N-diethylaminoethylmethacrylate (DEAM)	105-16-8	Monomer	"	2.0[d]	6.1[d]
Ethylene glycol (EG)	107-21-1	Impurity in HEMA and hydrolysis product	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**0.54**	**1.6**
Diethylene glycol (DEG)	111-46-6	Impurity in HEMA and 3ED; hydrolysis product	"	< 0.47	< 1.4
Ethylene glycol monoacetate (EGMAc)	542-59-6	Impurity in HEMA	"	**0.61**	**1.8**
Triethylene glycol (TEG)	112-27-6	Impurity in 3ED and hydrolysis product	"	**0.54**	**1.6**
[redacted]					

Table 4. Exposures to All Components of the FCS, Cont'd.

Substance	CAS Reg. No.	Function	Exposure Estimation Method	DC (ppb)	EDI (µg/p/d)
Methacrylic acid (MAA)	79-41-4	Impurity in [redacted] and HEMA; hydrolysis product	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**0.29**	**0.88**
Ethylene glycol dimethacrylate (EGDMA)	97-90-5	Impurity in 3ED	"	< 0.15	< 0.45
[redacted]					
Triethylene glycol dimethacrylate (3ED or TEGDMA)	109-16-0	Monomer	Msmt. in aqueous dispersion of FCS, 100% migration calc.	0.087	0.26
Diethylene glycol monomethacrylate (DEGMMA)	2351-43-1	Impurity in HEMA	"	**0.051**	**0.15**
[redacted]					
Diethylene glycol dimethacrylate (DEGDMA)	2358-84-1	Impurity in HEMA and 3ED	Msmt. in aqueous dispersion of FCS, 100% migration calc	**< 0.013**	**< 0.040**
[redacted]					
C8-C10 perfluorinated compounds	--	--	Msmt. in FCS	[redacted]	
[redacted]					

[a]Our values are slightly lower than the notifier's because the notifier assumed an FCS use level of 1.27 wt-% on paper in the calculation rather than the requested 1.2 wt-% use level.

[b]Our values are higher than the notifier's by two orders of magnitude because the notifier 1) neglected to covert µg/in^2 to µg/g food by dividing by 10, and 2) incorrectly converted from µg/g to ppb. In addition, the notifier included alcoholic foods with the 10% ethanol results rather than with the 95% ethanol results.

[c]Our values are higher than the notifier's because the notifier neglected to include the paper basis weight correction factor of 1.55 in the calculation. In addition, the notifier used the migration value for 95% ethanol for all food types rather than the migration value for 10% ethanol for aqueous and acidic foods and the migration value for 95% ethanol for alcoholic and fatty foods.

[d]The notifier made the same errors as those described in footnote c above. In this case, however, the errors cancelled each other out.

[e]This substance is regulated in §176.170(a)(5) for use in manufacturing the monomers.

NOTIFICATION LETTERS

The language in the acknowledgment letter dated 3/21/06 is acceptable as written.

CONCLUSIONS

The exposures to the FCS and its impurities are summarized in Table 4 above. We have no questions.

/s/
/s/
Kristina E. Paquette, Ph.D.

[redacted]

ASAHI GLASS COMPANY FCN 604

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name 2-Propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester, polymer with 2-(diethylamino) ethyl 2-methyl propenoate, 2-hydroxyethyl-2-methyl-2-propenoate, and [redacted]

2. CAS Registry Number

863408-19-9

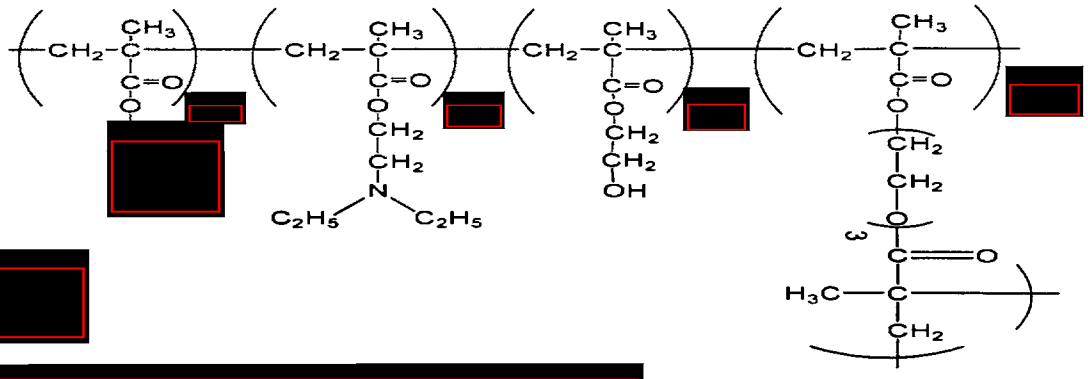
3. Trade or Common Name [redacted]

4. Other Chemical Names (IUPAC, etc.)

Copolymer of [redacted] 2-N,N-diethylaminoethylmethacrylate, 2-hydroxyethylmethacrylate,and 2,2'-ethylenedioxydiethyldimethacrylate

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



Mn = [redacted]
Mw =

Note: [redacted]

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

The IR spectrum may be found in Attachment 1 to FCN No. 599.

000006

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
[redacted]		
2-N,N-diethylaminoethylmethacrylate	105-16-8	Monomer
2-hydroxyethylmethacrylate	868-77-9	Monomer
2,2'-ethylenedioxydiethyldimethacrylate	109-16-0	Monomer
[redacted]		
Acetic acid	64-19-7	Processing aid
Acetone	67-64-1	Processing aid
Water	7732-18-5	Solvent

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

The manufacturing process details and reaction stoichiometry are found in Attachment 2 to FCN No. 599.

000007

Section B - MANUFACTURE - Continued

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (ppm)	Maximum Residual (ppm)
HEMA	**868-77-9**	**178**	**203**
DEAM	**105-16-8**	**137**	**264**

Ensure that exposures to these substances are addressed in Section II.G of this form.

000008

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value
N/A	

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches
Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications. **See Attachment 3 to FCN No. 599 for supporting data.**

Property	Max. Value	Min. Value	Individual Batch Values
Appearance (visual)	[redacted]		
Solids (%)			
Specific Gravity (g/mL)			
pH			
Viscosity (mPa · s)			
Molecular Weight (10,000 D M_w)			

000009

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

The maximum weight percentage of oligomers with MW < 2500 is 0.015%.

See Attachment 4 to FCN No. 599 for analytical data.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

This product is a 20% aqueous dispersion of a fluorinated methacrylate (the FCS) in water and is intended for use on paper or paperboard in contact with all types of food (aqueous, acidic, alcoholic, and fatty) in a single use scenario under conditions of use B through H. Use of the dispersion in wet end processing of, or as a coating on, paper/paperboard will result in a maximum coating concentration of 1.2 wt % of the FCS in finished paper/paperboard.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

000010

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
The product is a 20% aqueous dispersion of a fluorinated methacrylate (the FCS) in water and is intended for use on paper or paperboard in a single use scenario Use of the dispersion in wet end processing of, or as a coating on, paper/paperboard will result in a maximum coating concentration of 1.2 wt % of the FCS in finished paper/paperboard.	**All food types: aqueous, acidic, alcoholic and fatty (types I through IX)**	**Microwave susceptor packaging**

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

000011

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

The FCS is intended to impart oil, grease and water resistance to paper and paperboard. It may be added in the wet-end or at the size press in cationic and non-ionic systems.

See Attachment 5 to FCN No. 599.

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

Less than 1% by weight, as determined by thermogravimetric analysis at 230°C. See Attachment 1 to this FCN for details, and Attachment 6 to FCN No. 599 for additional supporting data.

000012

Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure
N/A	N/A	N/A

000013

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

000014

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

000015

Section F - MIGRATION LEVELS IN FOOD - Continued

Section F - MIGRATION LEVELS IN FOOD - Continued

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

See Attachment 2 to this FCN for 100% migration calculations.

000017

[redacted]

Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV).* If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty.

See Attachment 2 to this FCN for the EDI calculations.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

000018

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: August 1, 2006

From: Division of Food Contact Notifications, Chemistry Review Group 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 604:** AGC Chemicals Americas, Inc., through Pillsbury Winthrop Shaw Pittman, LLP. Perfluorinated grease-proofing agent based on [redacted] for use on paper/paperboard. Submissions dated January 23, 2006 (initial submission), March 8, 2006 (first response to deficiencies) and April 7, 2006 (second response to deficiencies).

To: Division of Food Contact Notifications, Regulatory Group 2
Attention: P. Honigfort, Ph.D.

AGC Chemicals Americas, Inc. (AGC), through their agent Pillsbury Winthrop Shaw Pittman LLC, submitted this food contact notification (FCN) to expand the use of the fluorinated copolymer produced by the polymerization of [redacted] 2-N,N-diethylaminoethyl methacrylate, 2-hydroxyethylmethacrylate, and 2,2'-ethylenedioxy diethyldimethacrylate (trade name [redacted]. The food contact substance (FCS) is intended to impart oil, grease, and water resistance to paper/paperboard intended for use in microwave heat-susceptor packaging, at a maximum use level of 1.2 wt-% of dry fiber, intended to contact all food types. The FCS comprises 20 wt-% of the commercially marketed formulation, which is an aqueous dispersion trade named [redacted]

Background

The FCS is the subject of FCN 599 (effective July 29, 2006),[1] submitted by AGC to impart oil, grease, and water resistance to paper/paperboard, at a maximum use level of 1.2 wt-% of dry fiber, intended to contact all food types under conditions of use B through H. The FCS was also the subject of AGCs [redacted]

Chemistry information contained in FDA Form 3480 (initial submission) is referenced from FCN 599. The only new chemistry information is stability data (Attachment 1 of the initial submission) and exposure estimates (Attachment 2 of the initial submission). The March 8, 2006 and April 7, 2006 submissions clarified the intended use of the FCS and contained additional information regarding impurities and their levels in the FCS. Suggested language for the FCS is contained in Attachment 4 (initial submission).

[1] Chemistry memorandum for FCN 599 dated May 31, 2006 (K. Paquette to P. Honigfort).

Identity

The identity of the FCS was reviewed in FCN 599 and is incorporated by reference into this FCN. The May 31, 2006 chemistry memorandum for FCN 599 (K. Paquette to P. Honigfort) is provided as Appendix 1 to this chemistry memorandum.

We have no questions on the identity of the FCS.

Manufacture

Information on the manufacture of the FCS is contained in FDA Form 3480, Section II.B (initial submission) and FCN 599. The manufacturing process was adequately described in Attachment 2 of FCN 599 and in the corresponding chemistry memorandum in Appendix 1. Specification sheets for each of the starting materials were provided in Attachment 3 (FCN 599). Raw materials used in the manufacture of the FCS, as taken from Section II.B.1 (initial submission), are tabulated below.

Table 1: Raw materials used in the manufacture of the FCS

Chemical Name	CAS Reg. No.	Function
[redacted]		
2-N,N-diethylaminoethyl methacrylate (DEAM)	105-16-8	Monomer
2-Hydroxyethylmethacrylate (HEMA)	868-77-9	Monomer
2,2'-Ethylenedioxy diethyldimethacrylate	109-16-0	Monomer
[redacted]		
Acetic acid	64-19-7	Processing aid
Acetone	67-64-1	Processing aid
Water	7732-18-5	Solvent

Impurities

In Section II.B.3, AGC listed HEMA (CAS No. 868-77-9) and DEAM (105-16-8) as impurities in the FCS. In FCN 599, AGC analyzed the finished aqueous dispersion of the FCS for 20 possible impurities, modeled the concentration of the radical polymerization initiator using the Arrhenius equation, and analyzed for [redacted] C8-C10 perfluorinated compounds, and [redacted] at our request as a result of [redacted] These impurities were not listed in the subject FCN. In the February 22, 2006 letter to AGC, K. McAdams noted that the impurities listed in FCN 599 were not listed in the subject FCN. The notifier's March 8, 2006 submission acknowledged that these impurities were present in the subject FCN.

Impurities in the FCS and the analytical results for 18 of these impurities (see Table 2, below) are discussed in the chemistry memorandum for FCN 599 (Appendix 1) and summarized in the

Consumer Exposure Section below. Two starting materials, acetone and acetic acid, are not included in Table 2 because acetone [redacted] (i.e., exposure is essentially zero), and acetic acid is affirmed as generally recognized as safe (GRAS) in 21 *CFR* 184.1005 (Acetic Acid).

We have no questions on the manufacture of the FCS.

Intended Use and Technical Effect

Information on the proposed use of the FCS is contained in Form 3480, Section II.D (initial submission) and the March 8, 2006 submission. Information on the technical effect is contained in Section II.D.3 (initial submission) and FCN 599.

The subject FCS will be used to impart oil, grease, and water resistance to paper/paperboard intended for use in microwave heat-susceptor packaging, at a maximum use level of 1.2 wt-% of dry fiber, intended to contact all food types. The FCS comprises 20 wt-% of the commercially marketed formulation, which is an aqueous dispersion trade named [redacted] and may be added in the wet-end or at the size press in cationic and non-ionic systems. The proposed use of the FCS is substitutional for the use of [redacted] C8-based perfluorinated grease-proofing agents.

The technical effect of the FCS was adequately demonstrated in Attachments 5 and 7 of FCN 599, and is described in the chemistry memorandum for FNC 599 (see Appendix 1).

We have no questions on the intended use and technical effect of the subject FCS.

Stability

Information on the stability of the FCS is contained in Form 3480, Section II.E and Attachment 1 (initial submission), and FCN 599.

The thermal gravimetric analysis (TGA) and differential thermal analysis (DTA) data provided in Attachment 6 of FCN 599 indicated that the FCS was stable under conditions of use B through H. During heating from 0-100.8°C for 141.8 min at an initial thermal ramp of 50°C/min, the mass loss of the FCS was only 0.14 wt.-%.

In [redacted] We would consider <1% loss to be insignificant. The temperature ramp used in AGC's thermograms was fairly slow (20°C/min) compared to the temperature ramp experienced during microwave cooking (food reaches 200°C in 1-2 min). The percent mass loss of the FCS would likely be much lower if the temperature ramp in the thermograms were more similar to that observed during actual microwave cooking. We therefore suggested that AGC conduct new TGAs at a more rapid temperature ramp that would mimic microwave heating. New TGAs were provided in Attachment 1 (initial submission) and

demonstrated that during heating from room temperature to 226.5°C for 2 min at an initial thermal ramp of 120°C/min, the mass loss of the FCS was 1 wt.-%. During heating from 229-230.1°C at a thermal ramp of 10°C/min, the mass loss of the FCS was also 1 wt.-%.

We have no questions on the stability of the FCS.

Migrant Levels in Food

AGC did not carry out migration studies in support of the proposed use. Rather, they estimated exposure assuming 100% migration to food (see the discussion below).

Consumer Exposure

In FCN 599, AGC used a tiered approach to estimate exposure to low molecular weight oligomers (LMWOs) of the FCS and impurities in the FCS. This is discussed in greater detail below.

Low molecular weight oligomers (LMWOs)

AGC calculated exposure to LMWOs based on the assumption of 100% migration to food. Using size exclusion chromatography (SEC) data (Attachment 4 of FCN 599) that demonstrated that oligomers of MW <2500 Dalton comprise 0.015 wt.-% of the FCS, the 1.2 wt.-% use level of the FCS in paper, a basis weight of 0.05 g paper/in^2, our standard assumption that 10 g food contacts 1 in^2 packaging, and a CF of 0.001 for microwave susceptor packaging, AGC calculated a dietary concentration (DC) of 10 ng/kg (or 10 pptr) corresponding to an estimated daily intake (EDI) of 30 ng/person/day. We calculated the same exposure using a basis weight of 26 mg/in^2 for popcorn bags and our standard assumption that 5 g food contacts 1 in^2 of microwave susceptor packaging.[2] In the chemistry memorandum on FCN 599, we calculated a DC of 0.45 µg/kg (0.45 ppb). This value would not be expected to significantly increase from the use proposed in the subject FCN.

Although the proposed use of the FCS is substitutional for the use of C8-based perfluorinated grease-proofing agents, [redacted] of the other grease-proofing agents. However, as noted in our chemistry memorandum on FCN 599, we believe that the use of the subject FCS will not result in an overall increase in exposure to perfluorinated oligomers of molecular weight ≤2500 Dalton.

Analysis of an aqueous dispersion of the FCS and 100% migration calculations for impurities

In FCN 599, AGC relied on a tiered approach for determining levels of impurities in the FCS. Impurity levels were determined using three methods: 1) in an aqueous suspension of the FCS, 2) based on extraction of FCS-coated paper with dichloromethane, and 3) based on migration testing. We note that both the extraction and migration studies carried out in FCN 599 do not support the

[2] These assumptions were used in the September 23, 2005 chemistry memorandum for FCN 518 (K. Arvidson to V. Gilliam).

proposed use of the FCS in microwave heat-susceptor packaging. Therefore, exposure to impurities from the proposed use will be based solely on residual levels determined in the aqueous dispersion of the FCS.

As indicated in the chemistry memorandum for FCN 599, the notifier initially analyzed several production batches of the aqueous dispersion of the FCS for all possible impurities by solid phase microextraction gas chromatography with flame ionization detection (SPME/GC/FID), GC/FID, GC with mass spectrometric detection (MS), or high-performance liquid chromatography (HPLC). The results were given on p. 17 of Attachment 1.A to the cover letter to FCN 599 (FDA Vol. 1).

Raw data supporting these measurements were provided in Attachment 2 to the cover letter to FCN 599 (FDA Vol. 1) and in Attachments 3.G and 3.H to FCN 599 (FDA Vol. 7). However, we were unable to reproduce the results obtained by the notifier from the raw data provided. In the notifier's March 8, 2006 and April 7, 2006 responses to K. McAdams March 8, 2006 and March 21, 2006 deficiency letters, AGC provided sufficient raw data to enable us to complete the calculations for each impurity.

As indicated in the chemistry memorandum for FCN 599, AGC used the standard addition method and the calibration curve method to determine residual levels of impurities in the FCS. A review of the raw data indicated some discrepancies between levels reported by the notifier and levels we calculated. Residual levels of FCS components in the aqueous dispersion of the FCS, their concentration in food assuming 100% migration, and exposure estimates are summarized in Table 2, below. (Columns 1 through 3 in the following table are similar to Table 1 in the chemistry memorandum on FCN 599.)

Table 2: Residual levels of FCS components in the aqueous dispersion of the FCS and exposure estimates to these components

Substance	Function	Corrected mean conc. in aqueous dispersion (ppm)	DC[a] (ng/kg or pptr)
[redacted]			
2-diethylamino ethanol (DEAE)	Impurity in DEAM	290.7	91
[redacted]			
2-hydroxyethylmethacrylate (HEMA)	Monomer	184.9	58
2-N,N-diethylaminoethyl methacrylate (DEAM)	Monomer	134.1	42

Ethylene glycol (EG)	Impurity in HEMA and hydrolysis product	36.3	11.5
Diethylene glycol (DEG)	Impurity in HEMA and 3ED; hydrolysis product	<31.5[b]	<9.8
Ethylene glycol monoacetate (EGMAc)	Impurity in HEMA	40.4	12.5
Triethylene glycol (TEG)	Impurity in 3ED and hydrolysis product	35.9	11
[redacted]			
Methacrylic acid (MAA)	Impurity in C6FMA and HEMA; hydrolysis product	19.6	6
Ethylene glycol dimethacrylate (EGDMA)	Impurity in 3ED	9.4[c]	3
[redacted]			
Triethylene glycol dimethacrylate (3ED or TEGDMA)	Monomer	5.8	2
Diethylene glycol monomethacrylate (DEGMMA)	Impurity in HEMA	3.4	1
[redacted]			
Diethylene glycol dimethacrylate (DEGDMA)	Impurity in HEMA and 3ED	<0.89[d]	<0.3
[redacted]			
C8-C10 perfluorinated compounds	--	[redacted]	

[a] Based on a use level of 1.2 wt-% FCS in the finished paper, a concentration of 20 wt.-% FCS in the aqueous dispersion, a paper basis weight of 26 mg/in^2 for popcorn bags, our standard assumption that 5 g food contacts 1 in^2 microwave susceptor packaging and a CF of 0.001 for microwave susceptor packaging.
[b] Below the LOD of the analytical method.
[c] Detected at a level of 9.4 ppm (based on the x-intercept of the standard addition curve), which was below the LOQ of the analytical method of 10.1 ppm.
[d] Detected but below the LOQ of the analytical method.

Cumulative Exposure

On June 13, 2006, Toxicology asked for cumulative exposure information on DEAM and DEAE, two impurities in the FCS. In an e-mail dated June 20, 2006 (provided as Appendix 2 to this chemistry memorandum), we indicated that the most current cumulative DC (CDC) for DEAM is 2 ppb (based on FCN 599), and for DEAE is 36 ppb (based on FCNs 206, 311 and 338). The DC for DEAM and DEAE from the subject FCN is 42 pptr and 91 pptr, respectively. Because use of the subject grease-proofing agent is substitutional for uses of the grease-proofing agents that were the subject of FCNs 206, 311, 338 and 599, and exposure to DEAM and DEAE from the subject FCN are lower than the cumulative exposures determined for the previous four FCNs, the CDC (and CEDI) for DEAM and DEAE remains unchanged at 2 ppb (6 ug/p/d) and 36 ppb (110 ug/p/d), respectively.

We have no questions on consumer exposure.

Notification Language

The April 13, 2006 acknowledgment letter, as signed off by Chemistry on April 17, 2006, is appropriate as written.

Conclusion

We have no questions on this FCN.

/s/ [redacted]
Sharon Elyashiv-Barad, Ph.D.

[redacted]

Memorandum

Date: May 31, 2006

From: Division of Food Contact Notifications
Chemistry Group I, HFS-275

Subject: FCN 599: AGC Chemicals Americas, Inc., through Pillsbury Winthrop Shaw Pittman, LLP, submissions of 12/30/05, 3/1/06, and 3/22/06. Perfluorinated grease-proofing agent based on C-6 chemistry for use on paper/paperboard.

To: Division of Food Contact Notifications
Regulatory Group II, HFS-275
Attn: P. Honigfort, Ph.D.

AGC Chemicals Americas, Inc. (AGC), through Pillsbury Winthrop Shaw Pittman LLC, has submitted a food contact notification (FCN) for use of the fluorinated copolymer produced by the polymerization of [redacted] 2-N,N-diethylaminoethyl methacrylate, 2-hydroxyethylmethacrylate, and 2,2'-ethylenedioxy diethyldimethacrylate (trade name [redacted]) to impart oil, grease, and water resistance to paper/paperboard, at a maximum use level of 1.2 wt-% of dry fiber, intended to contact all food types under conditions of use B through H. The food-contact substance (FCS) comprises 20 wt-% of the commercially marketed formulation, which is an aqueous dispersion trade named [redacted] The FCS is not currently authorized for any uses in or on food. The FCS was the subject of prenotification consultations [redacted] with AGC.

IDENTITY, MANUFACTURE, AND COMPOSITION

A. Identity

Chemical Name and CAS Registry No.

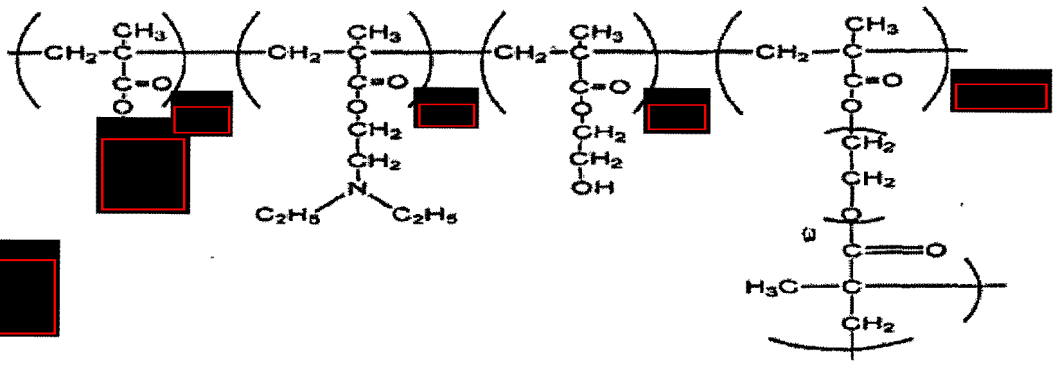
863408-19-9 — 2-propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester, polymer with 2-(diethylamino)ethyl 2-methyl propenoate, 2-hydroxyethyl-2-methyl-2-propenoate, and [redacted]

Common Names — copolymer of [redacted] 2-N,N-diethylaminoethylmethacrylate, 2-hydroxyethylmethacrylate, and 2,2'-ethylenedioxydiethyldimethacrylate

[redacted] (trade name for FCS)
[redacted] (developmental name for FCS)

[redacted] (trade name for aqueous dispersion)
[redacted] (developmental name for aqueous dispersion)

Structure



Mn = [redacted]
Mw = [redacted]

Ratios of monomer units are expressed in mole ratios.

The number average molecular weight (M_n) and weight average molecular weight (M_w) are typical values for the FCS as determined by size exclusion chromatography (SEC) with poly(methyl methacrylate) standards (see Attachment 4 to the FCN (FDA Vol. 7) for supporting data).

The notifier has demonstrated with the same SEC data that oligomers of molecular weight (MW) < 2500 comprise [redacted] of the FCS.

Physical Properties/Specifications (see Part II.C.2.a of Form 3480 and Attachment 3.A to the FCN (FDA Vol. 7))

Aqueous Dispersion	Appearance Percent solids Specific gravity (g/mL) pH Viscosity (mPa·s)	[redacted]
FCS	M_w (Daltons)	[redacted]

Data to Characterize the FCS

A Fourier transform IR spectrum of the dried FCS is given in Attachment 1 to the FCN (FDA Vol. 7).

The FCS is adequately identified.

B. Manufacture

The manufacturing process is adequately described in Attachment 2 to the FCN (FDA Vol. 7).

[redacted]

C. Composition

The notifier analyzed the finished aqueous dispersion of the FCS for 20 possible impurities, modeled the concentration of the polymerization initiator using the Arrhenius equation, and looked for [redacted] The analytical results for 18 of these impurities are given in Table 1 (see the detailed discussion below). A complete list of the impurities is given in Table 4. Two starting materials, acetone and acetic acid, are not included in the tables because 1) acetone [redacted] (i.e., exposure is essentially zero), and 2) acetic acid is affirmed as generally recognized as safe (GRAS) in 21 *CFR* 184.1005.

D. Stability

The thermal gravimetric and differential thermal analysis data provided in Attachment 6 to the FCN (FDA Vol. 7) indicate that the subject FCS is stable under the intended conditions of use.

[redacted]

INTENDED USE AND USE LEVEL

The FCS is intended to impart oil, grease, and water resistance to paper/paperboard intended to contact all food types under conditions of use B through H. The FCS may be added at the wet end or the size press during papermaking such that the total amount of the FCS in the finished paper/paperboard does not exceed 1.2 wt-% on a dry fiber basis. The FCS will be substitutional for other perfluorinated grease-proofing agents.

TECHNICAL EFFECT

The technical effect of the FCS in imparting oil, grease, and water resistance to paper/paperboard is adequately demonstrated in Attachments 5 and 7.A to the FCN (FDA Vol. 7). Results from the TAPPI "Kit" test and other measures of oil or water repellency consistently improved with increasing concentrations of the FCS applied to various paper samples at either the wet end or the size press.

TIERED APPROACH TO ESTIMATING EXPOSURE

A. Oligomers

The notifier calculated the concentration in food of low-molecular-weight oligomers (LMWO) of the FCS, assuming 100% migration to food and using the SEC data that demonstrated that oligomers of MW < 2500 comprise 0.015 wt-% of the FCS, the 1.2 wt-% use level of the FCS in paper, our average paper basis weight of 50 mg/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging (see Table 1):

$$\frac{0.00015 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.012 \text{ g FCS}}{\text{g paper}} \right| \frac{0.050 \text{ g paper}}{\text{in}^2} \left| \frac{\text{in}^2}{10 \text{ g food}} \right. = 9.0 \text{ µg/kg oligomers in food}$$

The notifier calculated the dietary concentration (DC) of the LMWO, using our recommended consumption factor (CF) of 0.05 for grease-proofed paper, and the estimated daily intake (EDI), assuming that individuals consume 3 kg of food per day. The results are summarized in Table 4. The calculations follow:

$$DC = (0.05 \text{ CF})(9.0 \times 10^{-9} \text{ g oligomers/g food}) = 0.45 \text{ ppb}$$

$$EDI = (0.45 \times 10^{-9} \text{ g oligomers/g food})(3000 \text{ g food/p/d}) = 1.4 \text{ µg/p/d}$$

Although the proposed use of the FCS is substitutional for the use of other perfluorinated grease-proofing agents, the [redacted] of the other grease-proofing agents. However, use of the subject FCS will not result in an overall increase in exposure to perfluorinated oligomers of molecular weight ≤ 2500 Da.

B. Analysis of Aqueous Dispersion of FCS and 100% Migration Calculations

The notifier initially analyzed several production batches of the aqueous dispersion of the FCS for all possible impurities by solid phase microextraction gas chromatography with flame ionization detection (SPME/GC/FID), GC/FID, GC with mass spectrometric detection (MS), or high-performance liquid chromatography (HPLC). The results are given on p. 17 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1).

Raw data supporting these measurements are provided in Attachment 2 to the cover letter to the FCN (FDA Vol. 1) and in Attachments 3.G and 3.H to the FCN (FDA Vol. 7). However, we were unable to reproduce the results obtained by the notifier from the raw data provided. In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided sufficient raw data to enable us to complete the calculations for each of the impurities (see pp. 2-4 of the cover letter and Attachment 1 to the 3/1/06 submission).

Standard Addition Method

AGC used the standard addition method to determine the residual level of several of the impurities in the FCS. This involved spiking the aqueous dispersion of the FCS with increasing concentrations of the impurity of interest and constructing a standard addition curve of instrument response vs. spiked solution concentration. The y-intercept (x=0) of this standard addition curve is the instrument response to the unspiked sample, and the x-intercept (y=0) is the concentration of the unspiked sample.[1] If the concentration of the impurity of interest is determined in several industry batches, a new standard addition curve would normally be constructed for each sample because the x- and y-intercepts in each case are unique.

AGC used the standard addition curve determined for one lot of the aqueous dispersion of the FCS to calculate concentrations in several lots, arguing that the matrices of the samples were the same. AGC divided the peak area of each unspiked sample (the "y-intercept") by the slope of the standard addition curve to obtain the concentration of the impurity in each lot. As was stated above, a different standard addition curve should have been generated for each sample because the x- and y-intercepts will be different for each.

Based on the conservatisms built into our exposure estimates, we accept AGC's argument that the slope is the same for all the curves determined for each impurity. However, AGC's calculation does not account for the changes in the x- and y-intercepts or the data scatter that would result from experimentally determining the standard addition curve for each lot. We were able to account for these factors by moving each data point of the standard addition curve vertically by an amount equal to the difference in instrument response between the unspiked sample of interest and the unspiked sample used to construct the original standard addition curve. In this manner, we defined the correct line for each lot and determined the residual concentration of the impurity in each lot from the resulting x-intercept.

We found that AGC's simplified method for calculating the impurity concentrations could have resulted in underestimates of exposure by up to a factor of 20. In the case of ethylene glycol monoacetate (EGMAc), AGC obtained a concentration of 0.7 mg/kg in Lot 50251 of the aqueous dispersion of the FCS (see Attachment 2.G to the cover letter to the FCN (FDA Vol. 1)). With our more rigorous calculation, the result was 12 mg/kg (the x-intercept of our standard addition curve).[2] We therefore found it necessary to recalculate all the impurity concentrations that were based on the standard addition method. Our averaged results for four

[1] See http://zimmer.csufresno.edu/~davidz/Chem106/StdAddn/StdAddn.html for a more detailed explanation.

[2] This lot was not included in the final average value for EGMAc.

lots (14-2, 17-1, 17-2, and 50351) of each impurity are included in Table 1 (see Attachment 1 to the 3/1/06 submission for AGC's results).

Table 1. Residual Levels of FCS Components in the Aqueous Dispersion of the FCS and Concentrations in Food, Assuming 100% Migration (Corrected Results Are Indicated in Bold)

Substance	Analytical Method Calculation	Conc. in Aqueous Dispersion (mg/kg)	Conc. in Food (µg/kg)[a]
FCS oligomers of MW <2500	--	0.015 wt-% of dry FCS	9.0[b]
2-Diethylamino ethanol (DEAE)	Standard addition	[redacted]	
Ethylene glycol (EG)	Standard addition		
Diethylene glycol (DEG)	Calibration curve		
Ethylene glycol monoacetate (EGMAc)	Standard addition		
Triethylene glycol (TEG)	Calibration curve		
[redacted]			
Methacrylic acid (MAA)	Standard addition		
Ethylene glycol dimethacrylate (EGDMA)	Standard addition		
[redacted]			
Triethylene glycol dimethacrylate (3ED or TEGDMA)	Calibration curve		
Diethylene glycol monomethacrylate (DEGMMA)	Calibration curve		
[redacted]			
Diethylene glycol dimethacrylate (DEGDMA)	Calibration curve		
[redacted]			
C8-C10 perfluorinated compounds	--		
[redacted]			

[a]Based on a use level of 1.2 wt-% FCS in finished paper, a concentration of 20 wt-% FCS in the aqueous dispersion, the average basis weight of food-contact paper of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging.

[b]Because SEC was conduced on the dry FCS, the 20 wt-% concentration of the FCS in the aqueous dispersion was not included in the calculation.

[redacted]

We note that AGC followed the standard addition method correctly in the analyses of [redacted] in that they generated standard addition curves for each sample and obtained the concentration from the x-intercept of each curve (see Attachments 2.V and 2.X to the cover letter to the FCN (FDA Vol. 2)).

Calibration Curve Method

AGC used a traditional calibration curve to convert peak areas to concentrations for the remaining impurities determined in the aqueous dispersion of the FCS. In each case, AGC forced the calibration curve through the origin and calculated the impurity concentrations by dividing the peak area of each sample by the slope of the calibration curve. We recalculated the correct linear functions, including y-intercepts, for these calibration curves and obtained much better statistical fits to the data than AGC did (see Attachment 1 to the 3/1/06 submission for AGC's results). Our averaged results for four lots (14-2, 17-1, 17-2, and 50351) of each impurity are included in Table 1.

It turned out that our calculated levels of the impurities in the aqueous dispersion of the FCS did not differ significantly from AGC's, with the exception of [redacted] which was twice that calculated by AGC. We found that the biggest changes occurred when the slope of the standard addition or calibration curve was high and/or the peak area for the sample was low. In many cases, the slope was very low and the peak area for the sample was relatively high. Also, averaging the results for the four production lots selected by AGC reduced the differences.

During our review of the raw data submitted in Attachment 1 to the 3/1/06 submission, we found that samples of the aqueous dispersion of the FCS had been diluted by 50% with methanol prior to analysis for six of the impurities (EGMAc, ethylene glycol, triethylene glycol, [redacted] methacrylic acid, and ethylene glycol dimethacrylate) without any indication that this dilution had been accounted for in the calculations. In the 3/22/06 response to your deficiency e-mail dated 3/8/06, the notifier provided a more detailed description of the analytical methods that demonstrated that the 50% dilutions had been accounted for. In the standard addition method, the spiking solutions were also diluted by 50%, and in the calibration curve method, the concentrations obtained from the calibration curve were doubled.

Polymerization Initiator and Its Breakdown Products

The notifier estimated the residual level of [redacted] polymerization initiator, in the aqueous dispersion of the FCS, using the Arrhenius equation to estimate decomposition (see p. 11 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1)). Three of the impurities listed in Tables 1 and 4 are decomposition products of the initiator: [redacted] which are discussed in a literature article [redacted] of the cover letter to the FCN (FDA

Vol. 2).[3] These were the major degradation products detected in an electron spin resonance (ESR) study of the initiator and comprised a total mass balance of 92 to 95% of the starting initiator in the following amounts: [redacted]

In analyses of the aqueous dispersion of the FCS, [redacted] were detected, while the [redacted] was not (exposure to [redacted] was later refined in a dichloromethane extraction study – see below). The fact that the [redacted] which contributed significantly to the mass balance of decomposition products, was [redacted] is strong evidence that the [redacted] We have therefore concluded that the Arrhenius equation does not need to be used to establish an upper limit to the concentration of the initiator in the FCS and that exposure to the initiator is essentially zero.

A fourth potential degradation product of the initiator, [redacted] which was listed as an impurity in [redacted] was not detected in the ESR study described in the literature article. The notifier stated in Attachment 2.R to the cover letter to the FCN (FDA Vol. 2) that the experimental conditions described in the literature article were "much more favorable to its generation" than the AGC polymerization reaction. We therefore agree with AGC that exposure to this substance is essentially zero.

Exposure Estimates

The notifier calculated the concentration in food of 15 of the 20 impurities determined by the above methods, assuming 100% migration of components of the FCS to food. The results are given in Table 1 (our corrected results are indicated in bold). The following is an example calculation for EGMAc, using its concentration in the aqueous dispersion of the FCS of [redacted] mg/kg (from Table 1), the 20 wt-% concentration of FCS in the aqueous dispersion, the 1.2 wt-% use level of the FCS in paper, our average paper basis weight of 50 mg/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging:

[redacted] $\frac{\text{1 g aq. dispersion}}{\text{0.20 g FCS}} \times \frac{\text{0.012 g FCS}}{\text{g paper}} \times \frac{\text{0.050 g paper}}{\text{in}^2\text{ paper}} \times \frac{\text{in}^2}{\text{10 g food}} =$ [redacted]

The DCs and EDIs for these impurities were calculated as described above for the oligomers (CF = 0.05). The results are given in Table 4 (our corrected values are indicated in bold). These values are conservative because they are based on measured levels of the impurities in the aqueous dispersion of the FCS and the assumptions that the impurities are completely retained throughout the papermaking process (which is highly exaggerative for cases in which the FCS is added at the wet end) and that they migrate 100% from paper to food.

[redacted]

C. Extraction of FCS-Coated Paper with Dichloromethane and 100% Migration Calculations

For the 6 impurities whose exposures as calculated above exceeded levels supported by the available toxicological data (plus [redacted] – at our request as a result of [redacted], the notifier extracted paper treated with the FCS into dichloromethane (DCM) under reflux conditions for 7 hr and then 16 hr and analyzed the extract for the impurities by GC/FID, GC/MS, or LC/MS. The results are given on pp. 18-19 of Attachment 1.A to the cover letter to the FCN (FDA Vol. 1), and the supporting raw data are given in Attachment 1.B (FDA Vol. 1).

In [redacted] we explained to AGC that DCM was not an appropriate solvent for total extraction of highly polar molecules [redacted] We also explained that the validation of the total extraction experiments, which consisted only of spike-and-recovery tests on the extracts, was not complete because it did not demonstrate that all of the impurity of interest was extracted from the paper. However, we agreed with AGC that, at a minimum, it is necessary to demonstrate that the extraction yielded results greater than or equal to those that would be obtained with a migration test conducted under the appropriate conditions for the intended use. AGC conducted appropriate migration tests on [redacted] The DCM extraction results are therefore validated.

Upon inspection of the raw data for the DCM extractions, we found that the sets of chromatograms given for [redacted] and [redacted] on pp. 112-118 and 120-125 of Attachment 1.B to the cover letter to the FCN (FDA Vol. 1) are identical, with [redacted] identified as the analyte peak on each of the chromatograms. In addition, the set on which [redacted] is labeled indicates that [redacted] was detected in both the 7- and 16-hr extracts of the paper sample treated with the FCS (see Figures 58 and 59 on pp. 123-124 of Attachment 1.B), while the final report indicates that [redacted] was not detected in these extracts (see p. 62 of Attachment 1.B). In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided the correct chromatograms for [redacted] and explained that [redacted] was detected in the extracts but below the limit of quantification (LOQ) of the analytical method (see pp. 4-5 of the cover letter and Attachment 4 to the 3/1/06 submission). We are satisfied with these data.

Exposure Estimates

The notifier calculated the concentration in food of 3 of the 6 impurities (plus [redacted] determined in this manner, assuming 100% migration of components of the FCS to food. The results are given in Table 2. We note that the basis weight of the paper used in the extraction studies was 32.26 mg/in^2. Because the FCS is added as a wt-% of the paper, higher migration would be expected per square inch of paper of a typical basis weight of 50 mg/in^2. The notifier therefore scaled up the concentrations in food by a factor of 1.55 (50 mg/in^2 / 32.26 mg/in^2 = 1.55) to account for this difference (see p. 15 of Attachment 1.A to the cover letter to

the FCN (FDA Vol. 1)). The DCs and EDIs for these impurities were calculated as described above. The results are given in Table 4.

Table 2. Results of Dichloromethane (DCM) Extraction of Paper Samples Coated with the FCS, Assuming 100% Migration of Impurities to Food

Substance	Conc. in DCM (μg/in^2)	Conc. in Food (μg/kg)[a]
[redacted]		

[a]Assuming that 10 g of food contact 1 in^2 of packaging. A factor of 1.55 was also applied to account for the low basis weight of the paper samples used in the extraction tests.
[b]Detected but below the LOQ of the analytical method.

These exposures were based on the LOQ of the analytical method used to determine the impurities. In each case, the impurity was detected but at a level below the LOQ. Unfortunately, a true limit of detection (LOD) was not established for the analytical method, so we cannot quantify a lower limit for the exposures. However, we can state that the exposures are less than those based on the LOQ.

D. Migration Testing (Part II.F.1 of Form 3480 and Attachment 7 to the FCN (FDA Vol. 7)

The remaining 3 impurities were determined via migration tests in which paper samples coated at the size press to contain 1.27 wt-% FCS (on a dry fiber basis) were immersed in 10% or 95% ethanol for 2 hr at 100° C, followed by 10 d at 40° C. The food simulants were then analyzed for the impurities by GC/MS. The results are given on pp. 1570-1571 of Attachment 7.B to the FCN (FDA Vol. 7).

We identified the following deficiencies in the raw data supporting the migration study:

1) In Table 9 of the spike-and-recovery validation data for 2-N,N-diethylaminoethylmethacrylate (DEAM) in 10% ethanol on p. 1586 of Attachment 7.B to the FCN, the "composite" or unspiked migration sample was reported to have an average DEAM concentration of 0.0403 μg/mL, and this value was subtracted from the measured concentrations of the spiked samples. The supporting chromatogram for the composite sample on p. 1620 of Attachment 7.B indicates that DEAM (ion 86) had a peak area of 9738 units, which is far below the 90,000 units shown to represent the LOQ of the method of 0.05 μg/mL for DEAM on the calibration curve shown on p. 1607 of Attachment 7.B. If no subtraction is made from the validation measurements, the percent recoveries become as high as 490%.

2) In Table 11 of the spike-and-recovery validation data for [redacted] in 95% ethanol on p. 1588 of Attachment 7.B to the FCN, values are reported for a "Level 4" spike. No supporting chromatogram was provided for this Level 4 spike. A chromatogram was provided for a "Level 3" spike on p. 1640 of Attachment 7.B. However, the peak area for [redacted] on this chromatogram was [redacted], which is comparable to the [redacted] shown to represent the LOQ of the method of [redacted] on the calibration curve shown on p. 1624 of Attachment 7.B. In addition, the [redacted] peak area is less than the [redacted] peak area given for the [redacted] "LOD spike" on p. 1638 of Attachment 7.B.

In the 3/1/06 response to your 2/8/06 deficiency letter, the notifier provided adequate responses to these deficiencies (see pp. 5-7 of the cover letter to the 3/1/06 submission). In the case of deficiency 1, the notifier explained that they had provided an "example" calibration curve that did not correspond exactly to the samples that were analyzed. The notifier provided the correct calibration curve for the samples in Attachment 5 to the 3/1/06 submission. In the case of deficiency 2, the notifier provided the correct chromatogram for the "Level 4" spike in Attachment 6 to the 3/1/06 submission and explained that "Level 3" data were not developed for [redacted] due to a sample work-up issue. We are satisfied with the raw data, chromatograms, calibration curves, and calculations supporting the migration studies.

The migration tests were adequately validated by spike-and-recovery analysis at the LOQ of the analytical method and at two spiking levels above the LOQ. The recoveries of the three impurities ranged from [redacted]

Exposure Estimates

The concentrations in food of the three remaining impurities are given in Table 3, and the exposures are given in Table 4. The following is an example calculation of the DC of [redacted] using the concentrations in food given in Table 3, the food-type distribution factors (f_T) for polymer-coated paper, the CF of 0.05 for grease-proofed paper, and the 1.55 scale-up factor to account for the low basis weight of the paper samples used in the migration study (see above):

DC[redacted] = (0.05 CF)(1.55 scale-up factor)[redacted]
= [redacted]

EDI[redacted] = [redacted] (3000 g food/p/d) = [redacted]

E. Other Potential Impurities

At our request in [redacted] the notifier analyzed the aqueous dispersion of the FCS or DCM extracts of paper treated with the FCS for [redacted] C8-C10 perfluorinated compounds, and [redacted] The concentrations in food of these substances, assuming 100% migration, are given in Tables 1 and 2. The exposures are summarized in Table 4.

Table 3. Highest Results of Migration Studies Conducted on Paper Samples Coated with the FCS into 10% and 95% Ethanol for 2 hr at 100° C, Followed by 10 d at 40° C

Substance	Conc. in Food Simulant ($\mu g/in^2$)		Conc. in Food ($\mu g/kg$)[a]
[redacted]			
2-hydroxyethylmethacrylate (HEMA)	10% EtOH	0.148	14.8
	95% EtOH	0.157	15.7
2-N,N-diethylaminoethyl-methacrylate (DEAM)	10% EtOH	0.170	17.0
	95% EtOH	0.395	39.5

[a]Assuming that 10 g of food contact 1 in^2 of packaging. A factor of 1.55 was applied to <M> to account for the low basis weight of the paper samples used in the migration tests.
[b]Detected but below the LOQ of the analytical method.

[redacted] was determined in the aqueous dispersion of the FCS by HPLC/MS with an LOD of 0.03 µg/mL in the dispersion and an LOQ of 0.1 µg/mL (see Attachment 2.V to the cover letter to the FCN (FDA Vol. 2)) and in the DCM extracts by LC/MS with an LOQ of 0.01 $\mu g/in^2$ paper that was established by Covance (see pp. 99-110 of Attachment 1.B to the cover letter to the FCN (FDA Vol. 1)). [redacted] was detected in the aqueous dispersion of the FCS at an extremely low level between the LOD and the LOQ. [redacted] was not detected at all in the DCM extracts, i.e., no peak was discernable from the background noise.

We conclude that exposure to [redacted] is essentially zero for the following reasons: 1) [redacted] was not detected in the DCM extracts, which provide a more realistic estimate of migration to food than measurements in the aqueous dispersion of the FCS, 2) an exposure estimate based on the very high LOQ established for the DCM extraction study would be artificially high, especially considering that the notifier also applied a correction factor to account for the low basis weight of the paper samples used in the study, and 3) an exposure estimate based on the extremely low level measured in the aqueous dispersion of the FCS and a 100% migration calculation would be two orders of magnitude below that estimated from the LOQ of the DCM extraction study.

A range of C8-C10 perfluorinated compounds, excluding the acids, was determined in the FCS by GC/MS (see Attachment 2.W to the cover letter to the FCN (FDA Vol. 2)). [redacted]

[redacted] was determined in the aqueous dispersion of the FCS by HPLC/MS/MS with an LOQ of [redacted] in the dispersion (see Attachment 2.X to the cover letter to the FCN (FDA Vol. 2)). [redacted] was detected at an extremely low level of 1.2 ng/mL in the dispersion (the higher of two production batches), which is below the LOQ. Since no other data were provided to demonstrate that [redacted] was not expected to migrate to food (e.g., DCM extraction data for paper samples treated with the FCS), we have estimated exposure to PFOA to be [redacted] assuming 100% migration of the 1.2 µg/kg determined in the aqueous dispersion of the FCS.

Table 4. Exposures to All Components of the FCS (Corrected Results Indicated in Bold)

Substance	CAS Reg. No.	Function	Exposure Estimation Method	DC (ppb)	EDI (µg/p/d)
FCS oligomers of MW <2500	--	--	SEC msmt., 100% migration calc.	0.45[a]	1.4[a]
[redacted]					
2-diethylamino ethanol (DEAE)	100-37-8	Impurity in DEAM	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**4.4**	13
[redacted]					
2-hydroxyethylmethacrylate (HEMA)	868-77-9	Monomer	Migration study	1.2[c]	3.5[c]
2-N,N-diethylaminoethylmethacrylate (DEAM)	105-16-8	Monomer	"	2.0[d]	6.1[d]
Ethylene glycol (EG)	107-21-1	Impurity in HEMA and hydrolysis product	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**0.54**	**1.6**
Diethylene glycol (DEG)	111-46-6	Impurity in HEMA and 3ED; hydrolysis product	"	< 0.47	< 1.4
Ethylene glycol monoacetate (EGMAc)	542-59-6	Impurity in HEMA	"	**0.61**	**1.8**
Triethylene glycol (TEG)	112-27-6	Impurity in 3ED and hydrolysis product	"	**0.54**	**1.6**
[redacted]					

Table 4. Exposures to All Components of the FCS, Cont'd.

Substance	CAS Reg. No.	Function	Exposure Estimation Method	DC (ppb)	EDI (µg/p/d)
Methacrylic acid (MAA)	79-41-4	Impurity in [redacted] and HEMA; hydrolysis product	Msmt. in aqueous dispersion of FCS, 100% migration calc.	**0.29**	**0.88**
Ethylene glycol dimethacrylate (EGDMA)	97-90-5	Impurity in 3ED	"	< 0.15	< 0.45
[redacted]					
Triethylene glycol dimethacrylate (3ED or TEGDMA)	109-16-0	Monomer	Msmt. in aqueous dispersion of FCS, 100% migration calc.	0.087	0.26
Diethylene glycol monomethacrylate (DEGMMA)	2351-43-1	Impurity in HEMA	"	**0.051**	**0.15**
[redacted]					
Diethylene glycol dimethacrylate (DEGDMA)	2358-84-1	Impurity in HEMA and 3ED	Msmt. in aqueous dispersion of FCS, 100% migration calc	**< 0.013**	**< 0.040**
[redacted]					
C8-C10 perfluorinated compounds	--	--	Msmt. in FCS	[redacted]	
[redacted]					

[a]Our values are slightly lower than the notifier's because the notifier assumed an FCS use level of 1.27 wt-% on paper in the calculation rather than the requested 1.2 wt-% use level.

[b]Our values are higher than the notifier's by two orders of magnitude because the notifier 1) neglected to covert µg/in^2 to µg/g food by dividing by 10, and 2) incorrectly converted from µg/g to ppb. In addition, the notifier included alcoholic foods with the 10% ethanol results rather than with the 95% ethanol results.

[c]Our values are higher than the notifier's because the notifier neglected to include the paper basis weight correction factor of 1.55 in the calculation. In addition, the notifier used the migration value for 95% ethanol for all food types rather than the migration value for 10% ethanol for aqueous and acidic foods and the migration value for 95% ethanol for alcoholic and fatty foods.

[d]The notifier made the same errors as those described in footnote c above. In this case, however, the errors cancelled each other out.

[e]This substance is regulated in §176.170(a)(5) for use in manufacturing the monomers.

NOTIFICATION LETTERS

The language in the acknowledgment letter dated 3/21/06 is acceptable as written.

CONCLUSIONS

The exposures to the FCS and its impurities are summarized in Table 4 above. We have no questions.

/s/
/s/
Kristina E. Paquette, Ph.D.

[redacted]

Appendix 2 to Chemistry Memorandum for FCN 604:
Cumulative Exposures to DEAM and DEAE as a Result of FCN 599

On 6/13/06, Toxicology asked for cumulative exposure information on 2-N,N-diethylaminoethylmethacrylate (DEAM) and 2-diethylamino ethanol (DEAE), two impurities in the FCS that is the subject of FCN 599. Below are the new cumulative exposures to these substances once FCN 599 becomes effective.

The cumulative exposure to DEAM is currently 0.14 ppb DC, 0.42 ug/p/d (based on FCNs 206, 311, and 338; see FCN 338, memorandum to the administrative file dated 5/30/03, K. Randolph). The exposure to DEAM from FCN 599 is 2.0 ppb DC, 6.1 ug/p/d. Use of the grease-proofing agent that is the subject of FCN 599 is substitutional for uses of the grease-proofing agent that was the subject of FCNs 206, 311, and 338. Because the exposure to DEAM from FCN 599 is higher than that calculated for FCNs 206, 311, and 338, it becomes the new cumulative exposure.

The new cumulative exposure to DEAM therefore increases to 2.0 ppb DC, 6.1 ug/p/d. The cumulative exposure to DEAE is currently 36 ppb DC, 110 ug/p/d (based on FCNs 206, 311, and 338; see FCN 338, memorandum to the administrative file dated 5/30/03, K. Randolph). The exposure to DEAE from FCN 599 is 4.4 ppb DC, 13 ug/p/d EDI. Because use of the subject grease-proofing agent is substitutional for uses of the grease-proofing agent that was the subject of FCNs 206, 311, and 338 and exposure to DEAE from FCN 599 is lower than the cumulative exposure determined for the previous three FCNs, the cumulative exposure to DEAE remains 36 ppb DC, 110 ug/p/d.

I will add this e-mail to the Final folder in FARM for FCN 599.

Kristina E. Paquette, Ph.D.

Chemist
FDA/CFSAN/OFAS/DFCN
University Station, Rm. 2108
HFS-275
(301) 436-1232

ASAHI GLASS COMPANY FCN 1186

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Butanedioic acid, 2-methylene-, polymer with 2-hydroxyethyl, 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, sodium salt

2. CAS Registry Number

1345817-52-8

3. Trade or Common Name

(b) (4) (polymer)

4. Other Chemical Names *(IUPAC, etc.)*

(b) (4) (15% aqueous solution); (b) (4) (15% aqueous solution)

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a fluorinated copolymer produced by the polymerization of 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate, 2-hydroxyethylmethacrylate, 2-methylpropenoic acid, and 2-methylene-butanedioic acid.

Please see Attachment 1 for a structural diagram and a more complete description of the FCS.

Please see Attachment 2 for a report on size exclusion chromatography analysis of the FCS.

[X] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Please see Attachment 3 for IR spectra of the FCS.

[X] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
2-propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro octyl ester	2144-53-8	monomer	☒ Yes ☐ No
2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester	868-77-9	monomer	☐ Yes ☒ No
2-Methylpropenoic acid	79-41-4	monomer	☒ Yes ☐ No
Butanedioic acid, 2-methylene-	97-65-4	monomer	☒ Yes ☐ No
(b) (4)			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☒ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

†

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

Please see Attachment 4 for a description of the manufacturing process for the FCS.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE *(continued)*

See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
2-propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro octyl ester	2144-53-8	(b) (4)		☒ Yes ☐ No
2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester	868-77-9			☐ Yes ☒ No
2-Methylpropenoic acid	79-41-4			☒ Yes ☐ No
Butanedioic acid, 2-methylene-	97-65-4			☒ Yes ☐ No
(b) (4)				☒ Yes ☐ No
				☐ Yes ☒ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☐ Yes ☒ No
				☐ Yes ☒ No
				☒ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

Four substances are identified above as "not expected to migrate from the FCS" because they could not be detected in samples of the FCS from four production lots. See Section II.F.2 of this Form 3480, and analytical reports included in Attachment 9. Nevertheless, dietary concentrations and EDIs were calculated for these substances, based on an assumption of 100% migration at the limits of detection. See Section II.G.3 of this Form 3480 and Attachment 10.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C - PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
Appearance (visual)	(b) (4)
Specific gravity at 25 deg. C	
pH at 25 deg. C	
Percent solid	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Glass transition temperature	none observed	none observed	none observed -- see Attachment 5

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C - PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

No oligomers below 1000 Daltons are detected in the food contact substance. Please see 3-batch size-exclusion chromatography (SEC) analysis contained in Attachment 6.

[X] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: [✔] Single Use [ ] Repeat Use

The FCS will be formulated into a 15% solution in water, which is how the FCS will be made available commercially, under the trade name AG-E080. The FCS is intended for use as an additive in paper and paperboard that may come into contact with all types of food under conditions of use B-H, as set forth in 21 C.F.R. § 176.170(c). The intended function of the FCS is to impart oil, grease, and water resistance to treated paper and paperboard articles. Use of the formulated solution in the wet end processing of paper, or as a coating applied at the size press, will result in a maximum concentration of 1.2% (by weight) of the FCS in the finished paper.

[ ] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
The FCS is used in paper and paperboard (i) during wet-end manufacture at levels not exceeding 1.2% by weight (of paper) and/or (ii) as a coating not exceeding 1.2% by weight (of paper)	All food types: aqueous, acidic, alcoholic and fatty (types I through IX)	B through H

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

Not applicable

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

The FCS is intended to impart oil, grease and water resistance to paper and paperboard. It may be added in the wet-end of the papermaking process or at the size press, in cationic and non-ionic systems. See Attachment 7 for data demonstrating the efficacy of the FCS for its intended use and the minimum amount of FCS (1.2%, based on the weight of paper) needed to achieve the intended technical effect.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

No degradation of the FCS is expected. Please see thermogravimetric data in Attachment 8.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
None. Please see thermogravimetric data in Attachment 8.			
STRUCTURE		**STRUCTURE**	
SUBSTANCE NAME	**CAS REG. NO.**	**SUBSTANCE NAME**	**CAS REG. NO.**
STRUCTURE		**STRUCTURE**	

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime (see Chemistry Recommendations, Appendix II, Part 4).

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D.3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Not applicable -- 100% migration assumption used.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable -- 100% migration assumption used.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Not applicable -- 100% migration assumption used.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable -- 100% migration assumption used.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

Four production batches of the FCS were analyzed for the presence of monomers and other potential impurities. Full reports on the analytical methods and results of these analyses are presented in Attachment 9. The results of the analyses, which are summarized below, were used to calculate worst-case dietary concentrations (also summarized below) for all potential impurities. These worst-case 100% dietary concentration calculations, and the associated EDI calculations, are presented in detail in Attachment 10.

	Impurity Concentration (ppm) (in 15wt% aqueous solution)									Dietary Conc. (ppb)
	10L Scale Product				50L Scale Product				4-lot average	
Lot No.	K-4		K-5		50111101L1		50111102L1			
	n=1	n=2	n=1	n=2	n=1	n=2	n=1	n=2		
FMA (CAS 2144-53-8)	(b) (4)									
HEMA (CAS 868-77-9)										
MA (CAS 79-41-4)										
IA (CAS 97-65-4)										

(b) (4)

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq}) + (M_{ac})(f_{ac}) + (M_{al})(f_{al}) + (M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Please see Attachment 10 for EDI calculations.

[X] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

[ ] Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*

See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
2-propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro octyl ester	2144-53-8	(b) (4)			
2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester	868-77-9				
2-Methylpropenoic acid	79-41-4				
Butanedioic acid, 2-methylene-	97-65-4				
(b) (4)					

Memorandum

Date: June 11, 2012

From: Division of Food Contact Notifications
Chemistry Team II

Subject: FCN 1186: AGC Chemicals Americas, Inc. submission dated April 6, 2012 for the use of butanedioic acid, 2-methylene-, polymer with 2-hydroxyethyl, 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, sodium salt as an oil, grease and water repellent for food-contact paper and paperboard articles.

To: Division of Food Contact Notifications
Regulatory Team I
Attn: Ken McAdams, M.S.

AGC Chemicals Americas, Inc., through Crowell & Moring LLP, submitted this food-contact notification (FCN) dated April 6, 2012 and an update dated 5/24/2012 for the use of the food-contact substance (FCS) butanedioic acid, 2-methylene-, polymer with 2-hydroxyethyl, 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, sodium salt as an oil, grease and water repellent for food-contact paper and paperboard articles.

Background

The FCS is not currently regulated nor is there an effective FCN for the use of this material in contact with food.

Identity

CAS Name: butanedioic acid, 2-methylene-, polymer with 2-hydroxyethyl, 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, sodium salt
CASRN: 1345817-52-8
Trade name: (b) (4) (polymer)
Other names: (b) (4) (15% aqueous solution); (b) (4) (15% aqueous solution)

Characterization

The notifier provided an IR spectrum of the FCS in Attachment 3 of the notification. Additional physical chemical properties for the FCS are on page 6 of form 3480. The IR spectrum is consistent with the structure of the FCS.

Manufacture

The notifier provided details of the manufacturing process in Attachment 4 of the notification.

The monomers 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate (CAS 2144-53-8), 2-hydroxyethyl methacrylate (CAS 868-77-9), 2-methylpropenoic acid (CAS 79-41-4), 2-methylidenebutanedioic acid (CAS 97-65-4), (b) (4) are charged into a reactor. (b) (4) The product is filtered, adjusted for concentration and packaged.

Intended Use/Use Level and Intended Technical Effect

The FCS is intended to impart oil, grease, and water resistance to food-contact paper and paperboard. The FCS is intended to contact aqueous, acidic, alcoholic and fatty foods (food types I through IX) under conditions of use B-H. The FCS is formulated as a 15% solution in water and used at the wet-end or at the size press of the papermaking process. The maximum use level of the FCS will be no greater than 1.2% (dry weight) in the finished paper. Data supporting the intended technical effect are in Attachment 7 of the notification.

Stability

The notifier states that the FCS is stable under the intended conditions of use. Thermogravimetric data supporting the notifier's claim are in Attachment 8 of the notification.

Migration Studies

The notifier did not conduct migration experiments in support of this notification; instead, they are relying on 100% migration calculations. Data supporting the claimed residue levels are in Attachments 2, 6, and 9 of the notification and in the 5/24/2012 update to the notification. The notifier's exposure calculations are presented in Attachment 10 and revised exposure estimates are in Attachment C of the 5/24/2012 update to the notification.

Oligomers of the FCS

The notifier did not provide migration data or 100% migration calculations for the oligomers of the FCS in the original submission. However, they did provide data from the analysis of the FCS by gel permeation chromatography (GPC). FDA typically calculates exposure to polymeric food-contact articles using the total quantity of oligomers with masses less than 1000 Daltons that migrate to food. For fluorinated materials, the FDA calculates a normalization factor for the difference in molecular weight between the hydrocarbon and fluorinated versions of the oligomers. In our deficiency letter to the notifier, we provided a rough estimate for the normalized cutoff for fluorinated oligomers of the FCS, 2200 Daltons. This value was based on the difference in molecular weight between C6FMA (433 g/mol) and its hydrocarbon analog (200 g/mol). In the 5/24/2012 update to the notification, the notifier disagreed with our estimate and provided a cutoff of 1695 Daltons (the notifier's calculations are shown in the updated comprehensive toxicological profile in Attachment D of the 5/24/2012 update).

We have refined our normalized cutoff value here. Using the weight percentages of the monomers in the polymer (C6FMA (b) (4), HEMA (b) (4) MA (b) (4), and IA (b) (4)) and their molecular weights (C6FMA (433), HEMA (130), MA (93%), and IA 175%)), we determined the mass of a polymer chain

that would give the appropriate weight percentage of each monomer (*i.e.*, IA 175/0.025 = 7000). Using this representative mass, the respective weight percentages of each monomer and their respective molecular weights, we calculated the number of each monomer incorporated into the representative 7000 Dalton polymer (*e.g.,* for C6FMA (7000*0.77)/433 = 13). Multiplying the number of each monomer in the 7000 Dalton polymer by their respective molecular weights and summing these values gives the molecular weight of the fluorinated polymer (7400 Daltons). Substituting the molecular weight of the hydrocarbon analog of C6FMA into the equation gives a mass of 4243 Daltons. Dividing 7400 by 4243 gives a normalization factor of 1745, very close to what the notifier provided.

From the data provided in Attachment 2 of the original submission, there are no oligomers with molecular weight at or below 1695 Daltons. Therefore, the notifier claims that there will be no exposure to the oligomers. In these cases, FDA would base exposure to the oligomers on a validated limit of detection for the method. However, the notifier has not provided an LOD for the method. Given that the notifier has not provided a validated LOD, we will rely on the lowest reported value in the GPC data, 1881 Daltons (0.0002%) for our exposure estimates of the oligomers, which is reasonable given our calculated cutoff of 1745 Daltons.

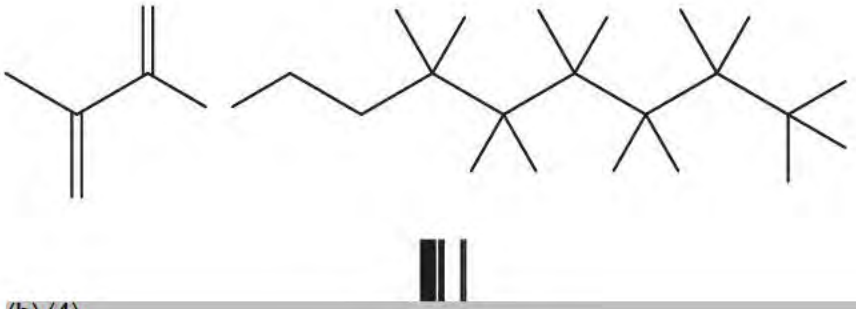
Impurities

The notifier diluted a 1 mL sample of the aqueous suspension of the FCS with 2 mL of 1 % acetic acid. To this mixture was added 1 mL of n-hexane and the mixture shaken and centrifuged for 10 minutes. The n-hexane layer was separated and diluted 500 times in n-hexane. The resulting solution was analyzed for 3,3,4,4,5,5,6,6,7,7,8,8,8-tetrafluorooctyl methacrylate (C6FMA), (b) (4) , methyl methacrylate (MMA), methyl isobutylate (MIB), and (b) (4) using GC/MS/MS and the standard addition method. The concentrations of the internal standards are presented in Table 1 and the concentrations of the analytes in the samples are presented in Table 2.

The notifier evaluated the FCS for MMA and MIB, which are not used in the production of the FCS but are most likely impurities in one or more of the starting materials. As MMA and MIB are impurities of impurities and not observed in any of the chromatograms, exposure to these materials can be considered to be zero. We will not discuss these compounds further.

In the 5/24/2012 update to the notification, the notifier provided mass spectra of the analytes supporting the identity of the chromatographic peaks and ions used in the quantitations. In Figures 1, 3, 5, and 7 of Attachment 9.2 of the notification, the notifier shows they quantified C6FMA using an m/z = 131. However, the mass spectrum of C6FMA presented in the 5/24/2012 update is annotated in such a way as to indicate that the ion used to quantitate C6FMA was m/z of 113. Given the totality of information in the notification, we are unable to determine if there is a simple typographical error associated with this data (113 for 131 or vice versa) or if the compound under goes an obscure rearrangement to give ion 131.

Although there is contradictory information regarding these analyses, we note that the peak identified as C6FMA in Figures 1, 3, 5, and 7 increases proportionately in size when known quantities of C6FMA are added to samples of the FCS as part of the standard addition method, supporting the notifier's choice to monitor ion 131. In addition, a peak with m/z 131 is also present in the mass spectrum of (b) (4) As such, we believe the notifier is using a viable ion for quantifying C6FMA.



(b) (4)

Table 1. Concentration of added standards in 1 mL of the FCS.

Analyte	Added concentration (ppm)			
	Vial 1	Vial 2	Vial 3	Vial 4
C6FMA	0	165	412	823
(b) (4)				
MMA	0	77.3	193	387
MIB	0	73.8	184	369
(b) (4)				

Table 2. Concentration of 6 impurities in the FCS using GC/MS/MS.

Analyte	Concentration (ppm)							
	Lot KA4		Lot KA5		Lot 50111101		Lot. 5011102	
	n=1	n=2	n=1	n=2	n=1	n=2	n=1	n=2
C6FMA	270	61	100	84	150	79	120	68
(b) (4)								
MMA	<<0.003	<<0.004	<<0.005	<<0.006	<<0.007	<<0.008	<<0.009	<<0.010
MIB	<<0.2	<<0.3	<<0.4	<<0.5	<<0.6	<<0.7	<<0.8	<<0.9
(b) (4)								

In addition to analyzing the FCS for the above 6 compounds, the notifier also analyzed the FCS for (b) (4) hydroxyethyl methacrylate (HEMA), (b) (4) methacrylic acid (MA), (b) (4) , itaconic acid (IA), (b) (4) using LC/MS/MS and the standard addition method.

One mL of the FCS (density: 1.08 mg/mL) was placed in each of four centrifugation vials and fortified with known quantities of each analyte. The concentrations of the internal standards are presented in Table 3 and the concentrations of the analytes in the samples are presented in Table 4.

(b) (4)

Table 3. Concentration of added standards in 1 mL of FCS

Analyte	Added concentration (ppm)			
	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)				
HEMA	0	49	97	146
(b) (4)				
MA	0	49	98	147
(b) (4)				
IA	0	232	463	695
(b) (4)				

Table 4. Concentrations of 8 additional impurities in the FCS

Analyte	Concentration (ppm)							
	Lot. KA4		Lot. KA5		Lot. 5011101		Lot. 5011102	
	n=1	n=2	n=1	n=2	n=1	n=2	n=1	n=2
(b) (4)								
HEMA	<15	<15	<15	<15	<15	<15	<15	<15
(b) (4)								
MA	520	470	610	730	660	750	590	620
(b) (4)								
IA	1900	1600	1800	1800	1700	1800	1800	1900
(b) (4)								

(b) (4)

presented in Table 5 and the concentrations of the analyte in the samples are presented in Table 6.

Table 5. Concentration of (b) (4) in 1 mL of FCS

Analyte	Added concentration (ppm)			
	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	0	0.005	0.009	0.014

Table 6. Concentration of (b) (4) in FCS.

	Concentration (ppm)			
	Lot. KA4	Lot. KA5	Lot. 5011101	Lot. 5011102
(b) (4)	<0.007	<0.007	<0.007	<0.007

(b) (4)

The FCS was analyzed for (b) (4) using LC/MS/MS and the standard addition method. (b) (4) The concentrations of the internal standard are presented in Table 7 and the concentrations of the analyte in the samples are presented in Table 8.

Table 7. Concentration of added (b) (4) in 1 mL of FCS.

Analyte	Added concentration (ppm)			
	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	0	23	46	70

Table 8. Concentration of (b) (4) in the FCS.

Analyte	Concentration (ppm)			
	Lot. KA4	Lot. KA5	Lot. 5011101	Lot. 5011102
(b) (4)	<<6	<<6	<<6	<<6

(b) (4)

The FCS was analyzed for (b) (4) using GC/MS/MS headspace analysis and the standard addition method. One-hundred µL of the FCS (density: 1.08 mg/mL) were placed in each of four centrifugation vials and fortified with known quantities of acetone. The concentrations of the internal standard are presented in Table 9 and the concentrations of the analyte in the samples are presented in Table 10.

Table 9. Concentration of added acetone in 100 µl of FCS.

Analyte	Lot	Added concentration (ppm)			
		Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	KA4, KA5	0	210	525	1049
(b) (4)	5011101, 5011102	0	105	262	525

Table 10. Concentration of (b) (4) in the FCS.

	Concentration (ppm)							
	Lot. KA4		Lot. KA5		Lot. 5011101		Lot. 5011102	
	n=1	n=2	n=1	n=2	n=1	n=2	n=1	n=2
(b) (4)	(b) (4)							

Exposure Estimates

The notifier provided exposure calculations in Attachment 10 of the notification and updated calculations in Attachment C of the 5/24/2012 update to the notification. Our exposure estimates are summarized in Table 11, below.

Oligomers

Using the value of oligomers below 1881 Daltons (0.0002%), the consumption factor for new polymers (0.05), the use level of the dry polymer on paper and the assumption that 100% of the oligomers migrate to food we estimate the dietary concentration (DC) of the oligomers to be 0.006 ppb. The estimated daily intake (EDI) of oligomers is calculated by multiplying the DC of 0.006 ppb by our standard assumption that a person consumes 3 kg of food per day, or 0.02 µg oligomers/p/d. The calculations are shown below.

$$DC=(0.05)\left(\frac{0.0002\text{ g oligomers}}{100\text{ g dry FCS}}\right)\left(\frac{1.2\text{ g dry FCS}}{100\text{ g paper}}\right)\left(\frac{0.05\text{ g paper}}{1\text{ in}^2}\right)\left(\frac{1\text{ in}^2}{10\text{ g food}}\right)\left(\frac{1000\text{ g food}}{1\text{kg food}}\right)\left(\frac{1000\text{ mg}}{1\text{ g}}\right)\left(\frac{1000\text{ µg}}{1\text{ mg}}\right)=\frac{0.006\text{ µg oligomers}}{\text{kg food}}$$

$$EDI=\left(\frac{0.006\text{ µg oligomers}}{1\text{ kg food}}\right)\left(\frac{3\text{ kg food}}{\text{person/day}}\right)=\frac{0.018\text{ µg oligomers}}{\text{person/day}}$$

Impurities

Exposures to the impurities in the FCS are calculated in the same fashion as the oligomers.

(b) (4)

Table 11. Exposure Estimates

	Acronym	CAS No.	Conc. in aq. FCS (ppm)	Conc. in Dry FCS (ppm)[1]	DC (ppb)	EDI (□g/p/d)
FCS oligomers < 1881 Daltons				0.0002 (%)	0.003	0.02
2-propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro octyl ester	C6FMA	2144-53-8	(b) (4)			
2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester	HEMA	868-77-9				
2-Methylpropenoic acid	MA	79-41-4				
Butanedioic acid, 2-methylene-	IA	97-65-4				
(b) (4)						

Cumulative Estimated Daily Intake

The FCS is not currently regulated or authorized for use in contact with food. Therefore, the EDI of 0.02 μg/p/d is the current cumulate EDI (CEDI).

Kirk B. Arvidson

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DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Kirk B. Arvidson, 0.9.2342.19200300.100.1.1=1300158954
Date: 2012.06.11 09:53:02 -04'00'

Kirk Arvidson, Ph.D.

HFS-275 (Chemistry Reading File)
HFS-275: KBArvidson:402-1152:FCN001186_C_MEMO: 6/8/2012; 6/11/2012
R/D Init: MAAdams:6/11/2012
Final: kba:6/11/2012

1 The concentration of the analyte in the aqueous suspension of the FCS is converted to its concentration in the dry FCS as follows: (117 mg C6FMA/1000 mL aq. FCS)(1 mL aq. FCS/1 g aq. FCS)(100 g aq. FCS/15 g dry FCS)(1000 g dry FCS/1 kg dry FCS) = 780 ppm C6FMA in the dry FCS.

ASAHI GLASS COMPANY FCN 1676

PART I – GENERAL INFORMATION *(Continued)*

6. List all PNCs, FMFs, correspondence letters, and FCNs not listed under item 7 that are relevant to this submission (use FDA assigned numbers, e.g., "PNC 099999")	Mark (X) if None ☒
7. If you previously submitted an FCN or FAP for this substance that is not effective or is effective but for a different use, enter the FCN or FAP number(s) assigned by FDA.	Mark (X) if None ☒

8. *For PNCs or FMFs* , provide a brief description of the information you have provided and state the purpose(s) of your submission *(or attach this description)* .

☐ See attachment number _____ in List of Attachments

PART II – CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE *See Chemistry Recommendations, Section IIA*

1. Chemical Abstracts Service *(CAS)* name

2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester, polymer with 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, sodium salt

2. CAS Registry Number

1878204-24-0

3. Trade or Common Name

(b) (4)

4. Other Chemical Names *(IUPAC, etc.)*

(b) (4)

5. Description

Attach a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide representative chemical structure(s) and the weight average (M_w) and number average (M_n) molecular weight. For new copolymers, provide the ratio of monomer units in the copolymer.

☒ See attachment number(s) 1 in List of Attachments

☐ See other FDA file _____

Notes:

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE *(cont.)* *See Chemistry Recommendations, Section II.A.*

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

☒ See attachment number(s) 2, in List of Attachments

☐ See other FDA file

Notes:

7. Molecular Weight Profile *(polymer FCSs only)*

Provide data that convey the molecular weight distribution, including a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons (low molecular weight oligomers, LMWOs), and report that percentage below. Analytical methods should be included.

Percentage oligomers below 1000 daltons: 0.000 % *(Ensure that consumer exposures to LMWOs are addressed under Section II.G of this form.)*

☒ See attachment number(s) 1,3, in List of Attachments

☐ See other FDA file

Notes:

8. Specifications

Attach a listing of physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. For new polymers, provide glass transition temperatures, intrinsic or relative viscosity, melt flow indices, morphology and crystallinity. Provide minimum or maximum specification limits or a range, as appropriate. In addition, include specification test results for at least three production batches of the FCS and the analytical methods for establishing compliance with specifications.

☒ See attachment number(s) 4,5, in List of Attachments

☐ See other FDA file

Notes:

SECTION B - MANUFACTURE *See Chemistry Recommendations, Section II.A. 4. a through c*

1. Manufacturing Process

Attach a description of the manufacturing process for the FCS, including reaction conditions *(e.g., amounts, times and temperatures)*, and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

☒ See attachment number(s) 6, in List of Attachments

☐ See other FDA file

Notes:

2. Manufacturing Ingredients

In Table 1 below, list all reagents, monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS. *Note: Because FDA systems will capture information entered on this form, you should list this information directly on the form, even if you choose to also include this information in an attachment.*

☐ See attachment number(s) in List of Attachments

☐ See other FDA file

Notes:

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION B - MANUFACTURE *See Chemistry Recommendations, Section II.A. 4. a through c*

TABLE 1: Manufacturing Ingredients

Chemical Name	CAS Reg. No.	Function	Is residual expected to remain in the final food contact material?**
3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctylmethacrylate	2144-53-8	Monomer	☒ Yes ☐ No
2-hydroxyethylmethacrylate	868-77-9	Monomer	☒ Yes ☐ No
2-propenoic acid	79-10-7	Monomer	☒ Yes ☐ No
(b) (4)			☐ Yes ☒ No
			☒ Yes ☐ No
			☐ Yes ☒ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

** If yes, include in Table 2. If no, support this conclusion in the manufacturing process description (#1 above).

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION C - IMPURITIES *See Chemistry Recommendations, Section II.A. 4.d and II.A.5*

1. Impurities

In the table below, enter impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Also attach supporting data for the residual levels, including analytical methods, and validation information. *Note: Because FDA systems will capture information entered on this form, you should list this information directly on the form, even if you choose to also include this information in an attachment.*

☒ See attachment number(s) 7, ☐ See other FDA file

Notes:

Substances identified below as "not expected to migrate" were not detected in samples of the FCS from four production lots. (See Attachment 7) Nevertheless, dietary concentrations and EDIs were calculated for these substances (See Section II.F.2 below)

TABLE 2: Impurities

Chemical Name	CAS Reg. No.	Typical Residual (%)	Maximum Residual (%)	Is migration to food expected?**
3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctylmethacrylate ("C6FMA")	2144-53-8			☒ Yes ☐ No
2-hydroxyethylmethacrylate ("HEMA")	868-77-9			☒ Yes ☐ No
2-propenoic acid ("AA")	79-10-7			☐ Yes ☒ No
(b) (4) [redacted]				☐ Yes ☒ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☐ Yes ☒ No
				☐ Yes ☒ No

** If yes, ensure that exposures to these substances are addressed under Section II.G of this form. If no, attach an explanation.

PART II – CHEMISTRY INFORMATION *(Continued)*

TABLE 2: Impurities

Chemical Name	CAS Reg. No.	Typical Residual (%)	Maximum Residual (%)	Is migration to food expected?**
(b) (4) [redacted]				☐ Yes ☒ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☐ Yes ☒ No
				☒ Yes ☐ No
				☐ Yes ☒ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

** If yes, ensure that exposures to these substances are addressed under Section II.G of this form.
If no, attach an explanation.

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION D - INTENDED USE *See Chemistry Recommendations, Section II.B. and II.C*

1. Intended Use

a. Indicate whether single or repeat use *(or both)* is intended: ☒ single use ☐ repeat use

b. Attach a description of the intended use (s) of the FCS. Include:

- Maximum use level (s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used *(e.g., films, coatings, molded articles)* and maximum thickness, as applicable.
- The food types (refer to food types in Table 1 of *Definitions of Food Types and Conditions of Use for Food Contact Substances*) expected to contact the FCS; include specific examples if known.
- The conditions of use: maximum temperatures and times of food contact (refer to conditions of use in Table 2 of *Definitions of Food Types and Conditions of Use for Food Contact Substances.*)

2. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

☒ See attachment number(s) 8, in List of Attachments

☐ See other FDA file

Notes:

3. Intended Technical Effect

Attach a description of the intended technical effect of the FCS. Attach data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect.

☒ See attachment number(s) 9, in List of Attachments

☐ See other FDA file

Notes:

The FCS is intended to impart oil, grease and water resistance to paper and paperboard. It may be added in the wet-end or at the size press in the paper manufacturing process. See Attachment 8 for data demonstrating FCS efficacy for its intended use.

SECTION E - STABILITY OF THE FCS *See Chemistry Recommendations, Section II.B. and II.D.2*

1. Stability of the FCS

Describe any degradation of decomposition (e.g., oxidation, photolysis, hydrolysis) or other chemical process expected as a result of the intended use of the FCS, either during its use in the manufacture of a food-contact article, or during migration testing (if performed) of a test plaque containing the FCS. Attach a description of any such processes.

☒ See attachment number(s) 10, in List of Attachments

☐ See other FDA file

Notes:

No degradation of the FCS is expected to occur. Please see thermogravimetric data in Attachment 10.

2. Degradation Products

In Table 3, enter any degradation or other products formed as a result of the use of the FCS, providing CAS names, CAS Reg. Nos. and attach structures as appropriate. Address the amount of any products that may migrate to food. Ensure that exposures to these substances are addressed in Section II.G of this form. *Note: Because FDA systems will capture information entered on this form, you should list this information directly on the form, even if you choose to also include this information in an attachment.*

☐ See attachment number(s) in List of Attachments

☐ See other FDA file

Notes:

No degradation of the FCS is expected to occur, as reflected in Attachment 9.

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION E - STABILITY OF THE FCS *(cont.)* *See Chemistry Recommendations, Section II.D.2*

TABLE 3: Degradation or Other Products Formed Due to the Use of the FCS

Chemical Name	CAS Reg. No.	Is migration to food expected?**
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No
		☐ Yes ☐ No

** If yes, ensure that exposures to these substances are addressed under Section II.G of this form.
If no, attach an explanation per instructions above.

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION F - MIGRATION LEVELS IN FOOD

Migration levels of the FCS or any substances *(such as impurities, oligomers, degradation products)* in food resulting from the intended use of the FCS may be estimated by migration testing or by calculation. See *Chemistry Recommendations, Section II.D.*

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime. See *Chemistry Recommendations, Appendix II, Part 4.*

1. Migration Testing Option *See Chemistry Recommendations, Section II.D. 1 through 3 and Appendix II*

a. Attach the full report of the migration tests, and include:

- A description of test specimen (s) , including full composition *(e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area)*, and relevant base polymer properties *(e.g., density, Tg, Tm, % crystallinity)* . Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side. See *Chemistry Recommendations section II.D.1.a and b.*

- Food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio *(e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in $_2$)* . If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in $_2$, provide evidence *(e.g., turbidity or precipitation data)* showing that saturation of the food simulant has not occurred. See *Chemistry Recommendations Section II.D.1.c,d.*

- Detailed descriptions of analytical methods, raw data *(e.g., peak areas)* , sample instrumental output *(e.g., chromatograms or spectra)* , and sample calculations relating the instrumental output to the migration values you report in mg/in $_2$, in Table 4. See *Chemistry Recommendations Section II.D.3.a-d.*

- A summary of the method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification *(spiking)* levels. Full details, including description of spiking procedure and calculations, must be included. See *Chemistry Recommendations Section II.D.3.e.*

☐ See attachment number(s) _____ in List of Attachments

☐ See other FDA file _____

Notes:

N/A -- 100% migration assumption used.

b. In Table 4, summarize results of migration testing for each test specimen. Give individual and average migration values *(mg/in$_2$)* for all analytes in each simulant at all time points. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components *(click here for example)* . See *Chemistry Recommendations section II.D.2*

☐ See attachment number(s) _____ in List of Attachments

☐ See other FDA file _____

Notes:

PART II – CHEMISTRY INFORMATION *(Continued)*

TABLE 4: Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and Time of Analysis	Migration *(each replicate)*	Average Migration *(average of replicates)*

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION F - MIGRATION LEVELS IN FOOD (cont.)

2. Migration Calculation Option

See Chemistry Recommendations, section II.D.5 for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modelling.

a. Was migration for certain migrants estimated by calculation? ☒ Yes ☐ No

b. Attach a description of the mathematical approach used and the basis for the approach in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

☒ See attachment number(s) 11,12, in List of Attachments

☐ See other FDA file _____

Notes:

SECTION G - ESTIMATED DAILY INTAKE *(EDI)* *See Chemistry Recommendations, Section II.E and Appendix IV*

The dietary concentration (DC) and EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. Single-Use Articles

In an attachment, show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/person/day
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: <M> is the concentration of the migrant in food; M_i is the migration value in simulant i; and (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty.

☒ See attachment number(s) 12, in List of Attachments

☐ See other FDA file _____

Notes:

2. Repeat-Use Articles

Using the migration levels to food determined in Section II.F and the repeat use scenario information described in Section II.D.2, show the calculations used for determining DC and EDI for the FCS and any migrants.

☐ See attachment number(s) _____ in List of Attachments

☐ See other FDA file _____

Notes:

PART II – CHEMISTRY INFORMATION *(Continued)*

SECTION G - ESTIMATED DAILY INTAKE *(EDI) (cont.)* *See Chemistry Recommendations, Section II.E and Appendix IV*

3. Summary of the Chemistry Information

In Table 5, enter the values for <M>, DC , and EDI of the FCS and any migrants, including oligomeric species (for unspecified oligomers, use the chemical name and CAS Reg. No. of the FCS) and degradation or other products. Provide CEDI to include this use.
Note: Because FDA systems will capture information entered on this form, you should list this information directly on the form, even if you choose to also include this information in an attachment.

☒ See attachment number(s) 11,12, ☐ See other FDA file _____

Notes:

TABLE 5: Summary of the Chemistry Information

Chemical Name	CAS Reg. No.	<M> *(µg/kg)*	DC *(µg/kg)*	EDI *(µg/p/d)*	CEDI *(µg/p/d)*
3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctylmethacrylate	2144-53-8	25.0	1.2	3.6	
(b) (4) [redacted]		32.6	1.6	4.8	
		5.28	0.3	0.9	
		1.2	0.06	0.18	
		0.72	0.036	0.11	
		1.2	0.06	0.318	
		115	5.8	17.3	
		2.5	0.13	0.4	
		.0072	.00036	.00108	

PART II – CHEMISTRY INFORMATION *(Continued)*

TABLE 5: Summary of the Chemistry Information

Chemical Name	CAS Reg. No.	<M> *(µg/kg)*	DC *(µg/kg)*	EDI *(µg/p/d)*	CEDI *(µg/p/d)*
(b) (4) [redacted]		0.46	0.023	0.069	
		0.072	0.0036	0.011	
		39.8	2.0	6.0	
		3.6	0.18	0.54	
2-Hydroxyethylmethacrylate	868-77-9	10.3	0.52	1.5	
2-Propenoic acid	79-10-7	2.64	0.13	0.39	
(b) (4) [redacted]		.0048	.0002	.0006	

Memorandum

Date: August 17, 2016

From: Division of Food Contact Notifications
Chemistry Review Team 2
Abigail E. Miller, Ph.D.

Subject: **FCN 001676**: Crowell & Moring LLP, on behalf of AGC Chemicals Americas, Inc. and Asahi Glass Company, LTD, 2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester, polymer with 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8- tridecafluorooctyl 2-methyl-2-propenoate, sodium salt as an oil, grease and water repellent for food-contact paper and paperboard at up to 1.2 % by weight of the finished paper. Submission received 5/16/16 (initial), 5/24/16 (chemistry studies) and 7/11/16 (amendment)

To: Division of Food Contact Notifications
Regulatory Team 2
Attn: K. McAdams, Ph.D.

Crowell & Moring LLP, on behalf of AGC Chemicals Americas, Inc. with Asahi Glass Company, LTD as the manufacturer, submitted this food-contact notification (FCN) for the use of the food-contact substance (FCS) 2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester, polymer with 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8- tridecafluorooctyl 2-methyl-2-propenoate, sodium salt as an oil, grease and water repellent for food-contact paper and paperboard at up to 1.2 % by weight of the finished paper in contact with all food types under Conditions of Use B-H.

Regulatory Background

This FCS is not regulated nor is it the subject of an effective FCN. We have several effective FCNs for similar polymers with the same fluorinated monomer. They are FCNs 599 & 604 (CASRN 863408-20-2 and 1225273-44-8), 885 &1027 (CARSN 1071022-26-8), 1186 (CASRN 1345817-52-8), and 1493 (1440528-04-0). AGR Chemicals and Asahi Glass are the notifier and manufacturer, respectively, for FCNs 599, 604, 1065 and 1186. With the exception of FCN 1065, all of AGR Chemicals FCNs listed above are for the use of fluorinated polymers as oil, water and grease repellants for use in paper and paperboard at up to 1.2 wt-%.

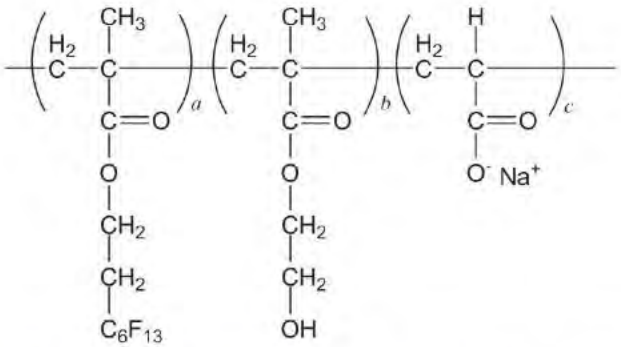
Chemistry Information. The chemistry information is included in Attachments 1-16, 57-64 and A-F. The initial submission, received May 16, 2016, was missing several attachments with chemistry information listed on Form 3480. Attachments 2, 3, 5, 8-12, and 15 were received May 24, 2016.[1] In response to the deficiency letter sent on June 24, 2016 the notifier submitted Attachment A-J on July 11, 2016.

1 The attachment numbers listed in the chemistry section (Part II) do match the attachment numbers listed in the List of Attachments (Part IV) of Form 3480. The Attachment numbers in Form 3480.IV match the names of the attachment files but the attachment numbers in the Form 3480.II match the headers in some of the Attachment documents. As an example, the file named "IntendedUse_(b) (4) _2016-05-05--(Attachment13-Form3480).pdf" in 3480.IV, has the header Attachment 8, Discussion of Intended Use in the document. Attachment 8 is listed in 3480.II.D.1 (Intended Use) rather than Attachment 13.

Identity

Identity information is contained in Form 3480.II.A and Attachments 1, 2, 4, 5 and A.

CAS Name:	2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester, polymer with 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8- tridecafluorooctyl 2-methyl-2-propenoate, sodium salt
CAS Number:	1878204-24-0
Trade Name:	(b) (4)) and (b) (4) solid polymer)
MW:	M_n = (b) (4) M_w = (b) (4) and M_z = (b) (4)
LMWO:	0.0001 %
Monomer ratio:	(b) (4)
Structure:	(from Attachment 1)



Characterization. The notifier provided a FTIR spectrum (Attachment 2) and a ^{13}C NMR spectrum (Attachment A) of the FCS. In the original submission, the notifier only included the IR spectrum. While the IR spectrum is consistent with the structure of the FCS, it is not enough to uniquely distinguish the FCS in the subject FCN from the FCS in effective FCN 1186. As the notifier for the subject FCN and effective FCN 1186 are the same, in response to our June 24, 2016 deficiency letter, the notifier submitted ^{13}C NMR spectra of three lots of both the subject FCS and the FCS from effective FCN 1186 so as to uniquely identify each substance. The peak identities are listed in Figure 3 of Attachment A. These data are consistent with the structures of the two FCSs.

Specifications. The notifier provided the specifications and characterization data for four lots (b) (4) of the FCS, appearance ((b) (4) , specific gravity (b) (4) pH (b) (4) and percent solids (b) (4) in Attachment 4. They were unable to determine the glass transition temperature of the FCS, as supported by the differential scanning calorimetry (DSC) scan supplied in Attachment 5.

We have no questions about the identity of the FCS.

Intended Use and Technical Effect

The intended use of the FCS is described in Attachments 13 and the analytical data to support the technical effect is reported in Attachment 14.

The FCS is intended for use as an additive in paper and paperboard that may come into contact with all types of food under conditions of use B-H. The FCS is added as a 25 % aqueous dispersion at either the wet-end or the size-press with a maximum use level of 1.2 % by weight of the finished paper. The FCS is not for use in contact with infant formula and human milk. Such uses were not included as part of the intended use of the FCS in the FCN.

The notifier provided data, in Attachment 14, to support the technical effect of the FCS as an oil, water and grease proofing agent in paper and paperboard. The data demonstrates that the technical effect of the FCS is self-limiting above 1.2 wt-%.

We have no questions about the intended use and technical effect of the FCS.

Stability

The thermogravimetric data, included in Attachment 15, demonstrates that the FCS loses less than 0.1 wt-% when heated to 120 °C. The notifier states that the FCS is stable under the intended conditions of use. As the highest temperature for condition of use B is 100 °C; we concur with the notifier's conclusion.

We have no questions about the stability of the FCS.

Manufacturing Process

The manufacturing process description and diagram are included in Attachment 6, and the starting materials are listed in Table 1 of Form 3480.

(b) (4) [redacted]

(b) (4) [redacted] is considered generally recognized as safe (GRAS) for direct addition to food under (b) (4) [redacted]. We will not discuss it further.

Certificates of Analysis and MSDSs for the starting materials (AA, C6FMA, HEMA, (b) (4) [redacted] (b) (4) [redacted]) are provided as Attachments 57-64 and B.

We have no questions about the manufacturing of the FCS.

Impurities

Residue levels and the identities of the impurities are reported in Form 3480.II.C and data supporting the residue levels of the impurities in the FCS are supplied in Attachments 3, 8, 9, 10, 11, 12, C, D, E, F and the July 11, 2016 response letter.

The impurities are: the low molecular weight oligomers < 1700 Da (LMWO), the starting monomers (C6FMA, HEMA and AA), the impurities in (b) (4) (b) (4) (b) (4) The full names, corresponding acronyms and residue levels for the impurities are listed in columns 2, 3, and 5 of Table 8, below.

LMWO

The notifier used gel permeation chromatography (GPC) with a refractive index detector to measure the molecular weight and the molecular weight distribution of the FCS as reported in Attachments 3 and C.

FDA typically calculates exposure to polymeric food-contact articles using the total quantity of oligomers with masses less than 1000 Daltons. For fluorinated materials, the FDA calculates a normalization factor for the difference in molecular weight between the hydrocarbon and fluorinated versions of the oligomers. We used the same method to calculate the normalization factor for the subject FCS as described in the chemistry memorandum for FCN 1186 (K. Arvidson to K. McAdams, June 11, 2012).

Using the weight percentages of the monomers in the subject FCS (b) (4)

1.7. We then multiple the normalization factor by the typical hydrocarbon LMWO threshold of 1000 Da and the LMWO threshold for this FCS is 1700 Da.

The GPC analysis, including the calibration curves and time slice tables, for three lots (b) (4) (b) (4)) of the dried FCS prior to reacting with (b) (4) is reported in Attachment 3.

(b) (4)

The GPC traces contain a small peak at a retention time of about 17.5 minutes, which corresponds to the expected retention peak range for LMWOs. The notifier did not account for this peak in their analysis of the LMWOs. In the June 24, 2016 deficiency letter, we asked the notifier to identify and quantify the substance responsible for this peak in the GPC trace. In the July 11, 2016 response, the notifier submitted a re-analysis of the three lots of dry FCS by GPC as Attachment C. The notifier included in Figure 1 of Attachment C a graph comparing the GPC traces of the dry FCS to a blank of both the initial and re-analysis. The notifier claims in their July 11, 2016 response letter that the peak is due to contamination of the solvent in the first GPC analysis and that if it was due to LMWOs the LMWOs would not produce a separate peak from the rest of the FCS as all the FCS was generated in the same polymerization reaction thereby producing a continuous distribution of polymer lengths. The peak height at 17.5 minutes in the re-analysis is on the same scale as the baseline noise in the blank traces. Therefore we conclude that the peak at 17.5 minutes in the initial analysis is likely from contamination of the solvent and is not associated with oligomers of the FCS.

From the results of the original analysis of the FCS for oligomeric materials, the notifier concluded that there are no oligomers below 2678 Da. The results from the re-analysis of the FCS indicate that there are no oligomers below 3693 Da. Therefore the notifier did not calculate the dietary intake of the LMWOs. As all six measurements produce a molecular weight distribution consistently above the LMWO threshold of 1700 Da, the notifier did not provide a validated limit of detection for the GPC method. As such we will use the lowest reported fraction in the time slice tables, 0.0001 %, as the fraction of LMWOs in the dry FCS.

Residue Levels of Impurities

The notifier provided a series of studies to quantify the residue levels of the impurities in the aqueous FCS. All of the analyses for the impurities, except for the characterization of the LMWOs, were completed using the method of standard addition. The standard addition curve is a plot of signal response as a function of the added concentration of the standard. The concentration of the impurities in the FCS is equal to the negative of the x-intercept (the ratio of the slope to the y-intercept) of the standard addition curve.

Four lots (b) (4) of the aqueous FCS were analyzed for the residue level of the impurities. Each lot was quantified twice. For the impurities that were either not detected or present at a level below the limit of quantitation, the notifier reported either the limit of detection (LOD) or the limit of quantification (LOQ) of the analytical method for the impurity as its residue level. Example calculations for the LOD of (b) (4) (b) (4) are shown in the July 11, 2016 response letter.

(b) (4)

A study report on the analysis for the residue levels of (b) (4) in the aqueous FCS by LC-MS/MS was supplied as Attachment 8.

A 1 mL sample of the aqueous FCS (density of 1.08 g/mL) is fortified with 0, 5, 10 or 15 µL of

an aqueous standard solution containing (b) (4) and (b) (4) (density 1.0 g/mL) then diluted to a total volume of 1.015 mL.

The added concentrations of the (b) (4) in the fortified samples are:

Table 1. added concentrations (ppm)

Analyte	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	0	96	193	289
	0	46	93	139

The notifier's added concentrations of (b) (4) and (b) (4), as reported in Table 3 of Attachment 8, are ~ 20 % lower than the values we calculated from the supplied method. We believe the notifier made an error in their calculations and have recalculated the concentrations. We will use our values to calculate the dietary intakes.

These solutions are mixed with 1mL of aqueous acetic acid and centrifuged. The supernatant is diluted 10 fold with water and analyzed by LC-MS/MS in multiple reaction monitoring (MRM) mode. The ion ranges monitored are reported on p3 and are consistent with the molecular weights of (b) (4). Example chromatograms are shown in Figures 1-8. The peak areas and standard addition curves for the four lots of the aqueous FCS are shown in Figures 9-12.

Linearity of the method is demonstrated for (b) (4) by R^2 values > 0.994 for three of the four lots and for (b) (4) by R^2 values > 0.991. For the lot with the highest residue level of (b) (4), the R values were 0.982 and 0.989.

(b) (4) was not detected above the LOD[3] of 16 ppm. The concentrations of (b) (4) in the four lots of the aqueous FCS are 1.6, 5.8, 1.2 and 1 ppm with an average concentration of 2.4 ppm.

C6FMA, (b) (4)

A study report on the analysis for the residue level of C6FMA, (b) (4) (b) (4) in the aqueous FCS by GC-MS/MS was supplied in Attachment 9. In their July 11, 2016 response to our June 24, 2016 deficiency letter, the notifier supplied a corrected version of the study report as Attachment D.

In our June 24, 2016 deficiency letter we asked the notifier to supply a total ion chromatogram and mass spectra data demonstrating that the chromatographic peaks and ions monitored are related to (actually represent) the assigned substances. In response, the notifier provided Attachment E. Attachment E contains a total ion chromatogram and mass spectra for the standards mixture. The standards mixture is used not only in the analysis of this FCS but also in the analysis of the FCSs in effective FCNs 599/604 and FCN 1186, per the July 11, 2016 response letter. Therefore, it includes not only C6FMA, (b) (4)

3 The notifier's reported LOD was 15 ppm. We rescaled is by a factor of 1.2 to account for the change in the standards concentrations used to calculate the LOD.

(b) (4) but 9 other substances not related to the subject FCS.

Although the retention times in the example total ion chromatogram presented in Attachment E are about five minutes shorter than those shown in the residue analysis reported in Attachment D, the total ion chromatogram supports the order of the retention times for C6FMA, (b) (4) (b) (4) and the mass spectra supports that the ions monitored are actually produced for each of the six substances.

In the June 24, 2016 deficiency letter, we asked the notifier about a peak at $t_R = 24.5$ min in the GC-MS chromatographic traces (labeled 4) assigned to (b) (4) for both the fortified samples and the FCS sample. In their July 11, 2016 response letter, they used the total ion chromatogram to support that the peak at $t_R = 24.5$ min is from (b) (4)[4]. We concur with the peak assignments. As the (b) (4) is not expected to be an impurity in this FCS, any peak in the chromatographic traces for the FCS sample is background noise or trace contamination of the instrument.

A 2 mL sample of aqueous FCS (density of 1.08 g/mL) is fortified with 0, 10, 20, 50 and 100 µL of a standard mixture in 2-propanol (density of 0.79 g/mL) containing 1.05 % C6FMA, 1.04 % (b) (4) 1.31 % (b) (4) 1.06 % (b) (4) 0.914 % (b) and 0.992 % (b) (4) and diluted to a final volume of 2.1 mL.

The added concentrations of the C6FMA, (b) (4) and (b) (4) in the fortified samples are:

Table 2. added concentrations (ppm)

Analyte	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5
C6FMA*	0	38	77	192	384
(b) (4)	0	38	76	190	380
	0	48	96	240	479
	0	39	78	194	388
	0	33	67	167	334
	0	36	73	181	363

*For C6FMA and (b) (4) the notifier did not always adhere to the concentrations listed in Table 2. For lot (b) (4), they used 0, 154, 308, 769, and 1538 ppm C6FMA for the first sample and 0, 77, 154, 385 and 769 ppm C6FMA for the second sample. For the first sample in lot (b) (4) they used added concentrations of 0 77, 192, and 384 ppm C6FMA. For (b) (4) for the first sample in lots (b) (4) and (b) (4) the notifier used added concentrations of 0, 76, 152, 379 and 759 ppm. These added concentrations are reported in Figures 4 (lot (b) (4) and 6 (lot (b) (4)). For C6FMA, the samples with the different added concentrations produced both the highest and lowest measured residue levels of the C6FMA but they are not outlier values. The residue levels of (b) (4) measured from the samples with the different added concentrations are comparable to those measured with the concentrations reported in Table 2. Therefore, we used all eight

4 (b) (4)

measurements to calculate the residue levels of C6FMA and (b) (4)

The fortified samples are mixed with aqueous acetic acid and the impurities extracted into n-hexane. The n-hexanes layer is removed, diluted 10 fold, and analyzed by GC-MS/MS.[5] The impurities are ionized by electron impact and monitored my MRM. The ion ranges monitored are reported on p3. Chromatograms, peak areas, and standard addition curves are provided as Figures 1-8.

Linearity of the method is demonstrated for (b) (4) by R^2 values >0.99. For (b) (4) and C6FMA the linearity of method is demonstrated by R values ranging from 0.953 to 0.998. While there is a wide range of R^2 values for the standard addition curves for C6FMA, the standard deviations of the x-intercepts of the standard addition curves are all lower than the standard deviations for the measurements between the lots. Therefore, the uncertainty in the linearity of the standard addition plots is subsumed by the variability in the quantity of the C6FMA in the different lots of the FCS. Only two of the R^2 values for (b) (4) are below 0.99 for the standard addition curves of C6AL and both of the associated residue levels are consistent with the rest of the measurements. Therefore, we are not concerned about the variability in the R^2 values and used all measurements to calculate the average residue level.

The average concentration for the six impurities in each lot of the aqueous FCS and the total average concentrations are:

Table 3. Concentrations in aq. FCS

Lot.	C6FMA	(b) (4)				
(b) (4)	63	189	27	<7	4	<<3
	195	119	13	<<2	<2	<<3
	55	95	<18	<<2	<2	<<3
	100	143	29	<7	4	9
Average	104	137	22	5	3	5

< indicates the measured residue level was below the LOQ.
<< indicates the measured residue level was below the LOD.

(b) (4) HEMA, (b) (4), AA, (b) (4)

A study report on the analysis for the residue levels of (b) (4), HEMA, (b) (4), AA, (b) (4) and (b) (4) by LC-MS was supplied in Attachment 10.

A 1 mL sample of aqueous FCS (density of 1.08 g/mL) is fortified with 0, 50, 100 and 150 µL of a standard mixture in water (density of 1.0 g/mL) containing 0.938 % (b) (4) 0.949 % HEMA, 1.01 % (b) (4) 1.01 % AA, 5.05 % (b) (4) and 0.128 % (b) (4) and diluted to a final volume of 1.15 mL.

5 The injection temperature of 220 °C is below the boiling point of some of the substances. This would be a problem for a typical analysis. However, for the method of standard addition known quantities of substances are added to a sample prior to processing and injection into the instrument. The amount of signal generated by the instrument is correlated with the amounts of standard added to the sample. Therefore, the issue is accounted for because the sample and standard are treated exactly the same.

The added concentrations of the [redacted] HEMA, [redacted] AA, [redacted] and [redacted] in the fortified samples are:

Table 4. added concentrations (ppm)				
Analyte	Vial 1	Vial 2	Vial 3	Vial 4
[redacted]	0	343	686	1029
HEMA	0	347	694	1041
[redacted]	0	369	739	1108
AA	0	369	739	1108
[redacted]	0	1847	3694	5541
[redacted]	0	47	94	140

When we checked the notifier's calculations, we found that added concentrations calculated using the method described on pages 1 and 2 of Attachment 10 and the concentrations and volumes in Tables 1 and 2 of Attachment 10 produced values 10 times higher than those reported by the notifier in Table 3 and Figures 2, 4, 6 and 8 of Attachment 10. Due to the inconsistency, we will use the higher added concentrations, shown in Table 4 above, for calculating the residue levels of the impurities in the FCS.

These fortified samples are mixed with 1 mL of aqueous acetic acid and centrifuged. The supernatant is diluted 50 fold with water and analyzed by LC-MS in single ion monitoring (SIM) mode. The ionization mode is electrospray in both positive and negative modes. The molecular ion peak was monitored for HEMA, [redacted] AA, [redacted] but not for [redacted]. In the June 24, 2016 deficiency letter, we asked why the notifier selected m/z= [redacted] for [redacted] as it corresponds to a mass value greater than the molecular weight o[redacted] In the July 11, 2016 response letter the notifier explained that [redacted] forms an adduct with sodium, to produce a positively charged ion. The sodium ion is already present in the FCS as a counter ion to the AA monomer in the FCS. Chromatograms, peak areas, and standard addition curves are included in Figures 1-8 of Attachment 10.

Linearity of the method is demonstrated by R^2 values from 0.92 to 0.999 for [redacted], and > 0.977 for [redacted] >0.998 for HEMA, > 0.996 for AA, and >0.986 for [redacted]. As all impurities in this study except for HEMA have residue levels below the LOQ and as such are not within the quantitation range, we are not concerned about the low values for R^2 for [redacted]

The average concentration for the six impurities in each lot of the aqueous FCS and the total average concentrations are summarized in Table 5, below.

Table 5. Concentrations in aq. FCS						
	EG	[redacted]	V601	AA	[redacted]	[redacted]
[redacted]	1880	530	<3	<110	<130	<0.6
	1920	440	<3	<110	<130	<<0.2
	1480	360	<3	<110	<130	<<0.2
	1320	370	<3	<110	<130	<<0.2
Average	1650	420	<3	<110	<110	<0.3

< indicates the measured residue level was below the LOQ.
<< indicates the measured residue level was below the LOD.

The LOQ and LOD were also rescaled by a factor of 10 to reflect the fact that the discrepancy in the notifier's reported added concentrations for standard addition could have been propagated to the samples used for determining the LOD and LOQ.

(b) (4)

A study report on the analysis for the residue level of (b) (4) in the aqueous FCS by headspace GC-MS/MS was supplied as Attachment 11.

A 100 µL sample of the aqueous FCS (density of 1.08 g/mL) is fortified with 0, 20, 50 and 100 µL of 0.101 % (b) (4) (b.p. 56 °C) then diluted with DMSO (density 1.1 g/mL) to a total volume of 400 µL.

The added concentrations of the (b) (4) in the fortified samples are:

Table 6. added concentrations of (b) (4)

Analyte	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	0	206	514	1029

The sample vials were heated at 85 °C for 60 minutes. Then, 250 µL of the headspace is injected into the GC-MS/MS. The (b) (4) is ionized by electron impact and monitored in MRM mode. The ion range monitored for (b) (4). Chromatograms and peak areas are included as Figures 1-4 of Attachment 11.

The linearity of the method is demonstrated for (b) (4) by R^2 values between 0.965 and 0.999. While there is a wide range of R^2 values of the standard addition curves, the relative standard deviation of the (b) (4) residue level in the FCS is only 18 % across all four lots. Therefore, we are not concerned about the variability in the R^2 values.

The concentration of (b) (4) in the four lots of the aqueous FCS is 532, 378, 525, and 522 ppm with an average of 489 ppm.

(b) (4)

A study report on the analysis for the residue level of (b) (4) in the aqueous FCS by LC-MS/MS was supplied as Attachment 12. In Attachment 12, there are five figures labeled 1, 2, 3, 7 and 8. There are no Figures 4-6. The data for quantifying the amount of (b) (4) in the four lots of the FCS analyzed in this study are supplied in Figures 1, 2, 3 and 7. We asked the notifier to clarify what information is presented in Figure 8 and explain how it is related to the analysis of (b) (4) in the FCS in our June 24, 2016 deficiency letter. In their July 11, 2016 response the notifier supplied an updated version of the study report as Attachment F, where they removed Figure 8 and labeled the data for quantifying the amount of (b) (4) in four lots of the FCS as Figure 1-4.

6 The difference in our value of 489 ppm and the notifier's value of 479 ppm is likely because they rounded the added concentrations of (b) (4) to 200, 500 and 1000 ppm for three of their standard addition curves shown in Figures 3 and 4 while we used the values reported in Table 6 of this memorandum with three significant figures for all the standard addition curves.

A 1 mL sample of the aqueous FCS (density of 1.08 g/mL) is fortified with 0, 50, 100 and 150 µL of 0.1 µg (b) (4) /L in water (density 1.0 g/mL) and diluted with water to a final volume of 1.15 mL.

The added concentrations of the (b) (4) in the fortified samples are:

Table 7. added concentrations of (b) (4)

Analyte	Vial 1	Vial 2	Vial 3	Vial 4
(b) (4)	0	4	9	14

These fortified samples are mixed with 1 mL aqueous acetic acid and 2 mL 2-propanol then centrifuged. The supernatant is diluted 10 fold with water and analyzed by LC-MS/MS in MRM mode. The ion range monitored for (b) (4) . Chromatograms, peak areas, and standard addition curves are included in Figures 1-4 of Attachment F.

Linearity of the method is demonstrated for (b) (4) by R^2 values >0.992.

(b) (4) was not detected in any of the four lots of the aqueous FCS above the LOD of 2 ppb.

We have no questions about the impurities in the FCS.

Exposure

The notifier did not conduction migration experiments and instead relied on the 100 % migration calculation for the LMWOs and all impurities. The notifier's calculations are provided in Attachment 16. The dietary concentrations (DC) are reported in Attachment 7.

LMWO

The notifier did not provide migration data or 100% migration calculations for the oligomers of the FCS in the original submission as they claim there are no LMWOs in the FCS.

As they did provide data from the analysis of the FCS by gel permeation chromatography (GPC), we will use the fraction of LMWOs < 1700 Da of 0.0001 %, to calculate exposure to the LMWOs as explained above (*Impurities, LMWOs*).

To estimate the DC of the LMWOs we used the following: the consumption factor for new polymers (0.05), the use level of the dry polymer on paper (1.2%), the percentage of LMWOs in the FCS (0.0001 % = 1 ppm), our standard assumption for the bases weight of paper and paperboard (0.05 g/in^2), our standard assumption that 10 g of food contacts 1 square inch of paper, and the assumption that 100% of the LMWOs migrate to food. The estimated daily intake (EDI) is calculated by multiplying the DC by our standard assumption that a person consumes 3000 g of food per day. The calculation is shown below.

$$DC=(0.05)\left(\frac{1\ \mu g\ LMWO}{1\ g\ dry\ FCS}\right)\left(\frac{1.2\ g\ dry\ FCS}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{1\ in^2}\right)\left(\frac{1\ in^2}{10\ g\ food}\right)$$

$$= \frac{0.000003\ \mu g\ LMWO}{g\ food} = 0.000003\ ppm = 0.003\ ppb\ LMWO$$

$$EDI = \left(\frac{0.000003\ \mu g\ LMWO}{1\ g\ food}\right)\left(\frac{3000\ g\ food}{person/day}\right) = \frac{0.009\ \mu g\ LMWO}{person/day}$$

Cumulative Exposure for LMWOs

We would typically state that the cumulative estimated daily intake (CEDI) for the LMWOs is equal to the EDI as this is a new FCS. However, for the subject FCN, we consider the exposure to the LMWOs from this FCS to be substitutional for the exposure calculated in FCN 1186 for the following reasons: 1) the intended use and use level in the subject FCN is exactly the same as that in effective FCN 1186, 2) the weight percentage of C6FMA in the two polymers is the same (b) (4) 3) the two polymers have the same or similar monomers, 4) the manufacturing process is the same as for FCN 1186 except for an [redacted] 5) the LMWO normalization factors are roughly equivalent for the two polymers, and 6) the residue levels of the LMWOs for both polymers are calculated from the lowest reported fraction in the time slice tables. The difference in the EDIs is because the lowest reported fraction in the time slice tables for FCN 1186 was 0.0002 % whereas it is 0.0001 % in the subject FCN, which is a negligible difference. Therefore, the mass fraction of C6FMA in the LMWOs for the two polymers is the same for the two polymers and the reported EDIs are substitutional for each other (FCN 1676, EDI= 0.009 µg/p/d and FCN 1186, EDI= 0.018 µg/p/d).

Impurities

To estimate the DC of the impurities the notifier used the following: the consumption factor for new polymers (0.05), the use level of the dry polymer on paper (1.2%), the percent solids in the aqueous dispersion containing the FCS (25 %), the residue level of the impurities in the aqueous dispersion containing the FCS, our standard assumption for the bases weight of paper and paperboard (0.05 g/in^2)), the our standard assumption that 10 g of food contacts 1 square inch of paper, and the assumption that 100% of the impurities migrate to food. The EDI is calculated by multiplying the DC by our standard assumption that a person consumes 3000 g of food per day. An example calculation using (b) (4) is shown below.

$$DC = (0.05)\left(\frac{489\ \mu g\ (b)\ (4)}{1\ g\ aq.\ FCS}\right)\left(\frac{1\ g\ aq.\ FCS}{0.25\ g\ dry\ FCS}\right)\left(\frac{1.2\ g\ dry\ FCS}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{1\ in^2}\right)\left(\frac{1\ in^2}{10\ g\ food}\right)$$

7 The FCS in effective FCN 1186 is a polymer containing [redacted] C6FMA and [redacted]-% HEMA, [redacted] MA (methacylate) and [redacted] IA (itaconic acid). The FCS in the subject FCN is a polymer containing (b) [redacted]-% C6FMA, (b) (4) HEMA and (b) [redacted] AA. As HEMA and IA are of similar molecular weights, as are AA and MA, then both the weight percentage of each type of monomer and the total number of each type of monomer in the two polymers is similar.

(b) (4) [redacted]

$$= \frac{0.0059\ \mu g\ \text{(b) (4)}}{\text{g food}} = 0.0059\ \text{ppm} = 5.9\ \text{ppb}\ \text{(b) (4)}$$

$$\text{EDI} = \left(\frac{0.0059\ \mu g\ \text{(b) (4)}\ e}{1\ \text{g food}}\right)\left(\frac{3000\ \text{g food}}{\text{person/day}}\right) = \frac{18\ \mu g\ \text{(b) (4)}}{\text{person/day}}$$

Table 8. Identities and Dietary Intakes of the Impurities.

	Substances	*Acronym*	*CASRN*	*Ave. conc. in aq. FCS (ppm)*	*DC (ppb)*	*EDI (µg/p/d)*
1	FCS oligomers < 1700 Da		Substitutional for LMWOs in FCN 1186			
2	2-propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro octyl ester	C6FMA	2144-53-8	104	1.3	3.7
3	2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester	HEMA	868-77-9	424	5.1	15
4	2-propenoic acid (acrylic acid)	AA	79-10-7	111	1.3	4.0
5	(b) (4)			136	1.6	4.9
6				130	1.6	4.7
7				1650	20	60
8				22	0.26	0.79
9				16	0.19	0.58
10				5	0.06	0.2
11				2.4	0.029	0.086
12				5	0.06	0.2
13				3	0.036	0.11
14				0.3	0.0036	0.011
15				0.002	0.000024	0.000072
16				3	0.036	0.11
17				489	5.9	18

The EDIs reported in Table 8, above, are conservative estimates of exposure because 1) they are calculated assuming 100 % migration of the impurities to food, 2) the EDIs for AA, (b) (4) (b) (4), and (b) (4) are calculated from either the LOD or the LOQ from the analytical method used to determine their residue levels, and 3) (b) (4) (b.p. 56 ^{o}C) is likely further volatilized during processing of paper through the steam rollers. We also note that the higher concentrations used to calculate the EDIs for (b) (4) HEMA, (b) (4), AA, (b) (4)

and (b) (4) are due to our corrections of the notifier's reported added concentration for the fortified samples.

Cumulative Exposure for Perfluorinated Impurities

The dietary intakes for the perfluorinated impurities in this FCN are less than or equivalent to those in FCN 1186. As the use described in effective FCN 1186 is substitutional for the use in this FCN, the exposures are substitutional and there will be no increase in exposure to the perfluorinated impurities: C6FMA, (b) (4)

Table 9. EDIs for perfluorinated impurities in FCNs 1186 & 1676

Substances	*EDI (µg/p/d)*	
	FCN 1186	*FCN 1676*
C6FMA	7	3.7
(b) (4)	6.3	4.9
	0.00042	0.000072
	0.0063	0.011

While the reported EDI for (b) (4) in the subject FCN (EDI=0.011 µg/p/d) is higher than that reported in FCN 1186 (EDI=0.0063 µg/p/d), the difference in the two values is due to a slight difference in the LOQs for the analyses.[9] Given that: 1) the residue levels of (b) (4) in both polymers were calculated from the LOQ for (b) (4) from the same analytical method, 2) (b) (4) is from the same source, an impurity in C6FMA monomer used in the manufacturing of both polymers, 3) the C6FMA is the same weight percentage in both polymers, and 4) the manufacturing processes is the same for both polymers in how it would affect the residue level of the (b) (4), the difference in LOQs are essentially within the error limits of the analysis and should be considered to be the same value. Therefore, there will be no increase in exposure to (b) (4) as a result of the authorization of this notification

We have no questions about the exposure estimates.

Notification Language

The notification language as written in the July 19, 2016 acknowledgement letter is adequate.

Comments

While we have sufficient information in the notification to support the dietary intakes reported in Table 8, it would be helpful for any future submissions to have the notifier address the discrepancy in the added concentrations for quantification of the levels of HEMA, (b) (4) AA, (b) (4). The additional information may help refine the CEDIs for these six substances.

9 The difference in LOQs is due to the noise level between the different measurements and possibly because of our corrections to the notifier's reported added concentration for the fortified samples.

Abigail E. Miller -S

Digitally signed by Abigail E. Miller -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001635697, cn=Abigail E. Miller -S
Date: 2016.08.17 12:31:45 -04'00'

Abigail E. Miller, Ph.D.

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HFS-275:AEMiller: 240-402-1224:FCN1676_C_memo.doc:AEM:Draft 7/24/16, 8/16/16
Init: Karvidson: 8/17/16
Final: AEM: 8/17/16

CHEMOURS FCN 885

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2-propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate

2. CAS Registry Number

1071022-26-8

3. Trade or Common Name

(b) (4) **CONFIDENTIAL**

4. Other Chemical Names *(IUPAC, etc*

Acetate salts of methacrylic acid copolymer with acrylic acid, diethylaminoethyl methacrylate, and 2-(perfluorohexyl)ethyl methacrylate

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The starting monomers used in the manufacture of the FCS are as follows:

CASRN	CAS Name	Common Name
2144-53-8	2-Propenoic acid, 2-methyl-, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester	2-Perfluorohexylethyl methacrylate (62-FMA)
105-16-8	2-Propenoic acid, 2-methyl-, 2-(diethylamino)ethyl ester	Diethylaminoethyl methacrylate (DEAM)
79-41-4	2-Propenoic acid, 2-methyl-	Methacrylic acid (MAA)
79-10-7	2-Propenoic acid	Acrylic acid (AA)

The molecular formula for the polymer is $(C_{12}H_9F_{13}O_2)_m (C_{10}H_{19}O_2N)_n (C_4H_6O_2)_o (C_3H_4O_2)_p$. The structural formula and quantitative composition of the polymer are given in **Attachment 1**.

Analysis of representative samples of the polymer by size exclusion chromatography (SEC) indicated weight-average molecular weights (Mw) of approximately (b) (4) For more details, see the analytical report set forth in **Attachment 2**.

The commercial product consists of an aqueous dispersion containing approximately 19.5% solids.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Representative IR and NMR (^1H and ^{13}C) spectra are provided in **Attachment 3**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
2-Perfluorohexylethyl methacrylate	2144-53-8	Monomer	☒ Yes ☐ No
Diethylaminoethyl methacrylate	105-16-8	Monomer	☒ Yes ☐ No
Methacrylic acid	79-41-4	Monomer	☒ Yes ☐ No
Acrylic acid	79-10-7	Monomer	☒ Yes ☐ No
(b) (4) CONFIDENTIAL			☐ Yes ☒ No
			☐ Yes ☒ No
			☒ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 4** for a description of the manufacturing process.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
2-Perfluorohexylethyl methacrylate	2144-53-8	See **Attachment 5**	(b	☐ Yes ☐ No (*)
Diethylaminoethyl methacrylate (DEAM)	105-16-8	See **Attachment 5**	(b)	☐ Yes ☐ No
Methacrylic acid	79-41-4	(b) (4)	–	☐ Yes ☐ No
Acrylic acid	79-10-7	(b) (4)	–	☐ Yes ☐ No
(b) (4)		See **Attachment 5**	(b	☐ Yes ☐ No
	(b) (4)	See **Attachment 5**	(b	☐ Yes ☐ No
	(b) (4)	(b) (4)	--	☐ Yes ☐ No
(b) (4)	(b) (4)	See **Attachment 5**	(b)	☐ Yes ☐ No
(b) (4)	(b) (4)	See **Attachment 5**	(b)	☐ Yes ☐ No
(b) (4)	(b) (4)-5	See **Attachment 5**	–	

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(*) The boxes in the right-hand column above are not checked because it is not certain whether migration of impurities will occur. Nonetheless, the maximum levels at which the compounds could migrate to food are calculated as noted in section II.F.2 below.

The impurity concentrations are expressed in terms of the concentration in the commercial product, i.e., the aqueous dispersion containing 19.5% solids. See **Attachment 5** for data on typical impurity levels at 19.5% solids.

(b) (4)

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† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
N/A	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Number-average molecular weight (Mn) (Daltons)	(b) (4)		
Solids Content (wt-%)			
Density (g/mL)			
pH			
Flash Point (°F)			
Viscosity (cP @ 23°C)			
Appearance			

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Additional specifications regarding maximum impurity levels are set forth in Section II.B.3 above; analytical methods for measuring impurity levels are discussed there. A table showing all applicable specifications, including both maximum impurity levels and physical property values, is set forth in **Attachment 12**. The relevant physical property specifications are reproduced in the table above, together with representative batch values. See **Attachment 13** for test methods used to determine compliance with the specifications identified above.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

Based on GPC analysis, the FCS is conservatively estimated to contain approximately 0.045% of low molecular weight oligomers (LMWO) below 2000 Daltons by weight of polymer solids. (Due to the fluorinated nature of the polymer, we have used 2000 Daltons rather than 1000 Daltons as the upper cut-off for determining the oligomer content to account for the comparatively high mass of the polymer relative to molecular size.) See **Attachment 2** for details of analyses conducted to determine the low molecular weight oligomer content.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☐ Repeat Use

The FCS copolymer is intended for use as an oil and grease resistant treatment for paper and paperboard intended for use in contact with food. The treatment may be applied either in the wet-end or at the size press. The copolymer is intended for use at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper.

The food-contact substance is intended to contact all types of food under Conditions of Use B through H and in susceptor microwave applications. The food-contact substance is intended for single-service use.

Suggested language for listing this FCN on FDA's "Inventory of Effective Food Contact Substance Notifications" is set forth in **Attachment 14**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
The FCS will be used to treat paper at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper.	All types of food (Types I through IX)	Conditions of Use B through H

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE
The FCS will be used to treat paper at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper.	All types of food (Types I through IX)	Susceptor microwave applications

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

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(b) (4) is intended to impart oil and grease resistance to paper and paperboard used in food-contact applications. The utility of the product as an oil and grease resistant treatment was measured using established paper industry performance test procedures. The grease resistance test (TAPPI test method T 559 pm-96) was performed on base and treated paper sheets to demonstrate performance efficacy (b) (4) (a description of this test is provided in FCN No. 206, Appendix VI). The application procedure and results are described below.

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Thirty-eight-pound base paper sheet was treated with sizing solution containing 4% ethylated starch (Penford Gums 280) and 2% (b) (4) at 158°F, using a laboratory size press. (Note: the application rate is expressed in terms of the commercial product, which contains approximately 19.5% of polymer solids. Thus, the paper was treated at a maximum level corresponding to 0.42% by weight of polymer solids on the paper.) The treated paper sheet was subsequently dried by a laboratory drum drier at 235°F. The dried paper contained (b) % fluorine. The treated paper sheet gave a repellency rating of 12, indicative of a high degree of grease repellency. The untreated base paper sheet gave a rating of less than 1. These results clearly demonstrate the technical effect delivered by (b) (4) as a grease resistance agent.

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For additional information on technical utility, see the Technical Information Sheet set forth in **Attachment 15**. Also included in **Attachment 15** is the Material Safety Data Sheet for the product.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

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(b) (4)

The thermal stability of the polymer has been evaluated in experiments that involved heating to temperatures up to 235°C to simulate the temperatures that may be reached during susceptor microwave cooking. A report of this testing appears in **Attachment 16**. The weight lost in heating a pre-dried polymer sample (b) (4) corresponded closely to the sum of known residuals and impurities (b) (4) implying no degradation or loss of the polymer itself. In addition, TGA-MS analysis of a polymer sample heated under the same conditions demonstrated that the mass fragments released in heating were consistent with residual monomers and other residuals present in the product. Finally, analysis of the polymer by ^{13}C-NMR before and after heating to 235°C did not indicate any change in the polymer structure. These data confirm the heat stability of the polymer under the conditions of its intended use.

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Part II – CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

(b) (4)

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration testing has not been carried out. Instead, worst-case migration of FCS oligomers and most potential impurities has been calculated based on measured levels in the product. See Section II.F.2 below.

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In addition, exhaustive extraction studies have been conducted on treated paper samples, and the resulting extracts analyzed to determine the levels of extractable perfluorohexylethyl methacrylate monomer (6-2 methacrylate),(b) (4) (b) in the finished paper. In this testing, paper samples treated at the size press with the FCS polymer at 0.42% by weight were Soxhlet extracted with chloroform for 6 hours, and the resulting extracts analyzed for the identified compounds. The same paper samples were subsequently extracted for 4 hours with fresh chloroform to generate additional extracts, which were analyzed to ensure that the impurities were exhaustively extracted.

As shown by the report in **Attachment 17**, the average levels of the three compounds measured in the initial extracts, and the corresponding concentrations relative to the paper sample surface area, were found:

Analyte	Average Concentration in Extract, ng/mL	Corresponding Amount in µg/in²
6-2 Methacrylate	(b) (4)	
(b) (4)		
(b) (4)		

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The second extraction yielded no additional detectable levels of the impurities. Thus, the initial 6-hour refluxing with chloroform achieved an exhaustive extraction of the treated paper for the compounds in question.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
N/A					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

No migration testing has been conducted, as stated previously. However, the exhaustive extraction testing described in **Attachment 17** was validated in accordance with FDA recommendations. See **Attachment 17** for details of the method validation.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

Due to space limitations, the worst-case migration calculations are set forth in **Attachment 18**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The worst-case migration levels calculated in **Attachment 18** may be multiplied by the applicable consumption factors (CFs) to calculate the corresponding concentrations at which FCS components may enter the diet. Because separate migration levels are calculated in **Attachment 18** for the use of the FCS under Conditions of B through H and in susceptor microwave applications, separate dietary concentrations are calculated for these two applications. For food-contact applications under Conditions of Use B through H, we use the CF of 0.05 that has been established previously for grease-proofing agents for paper and paperboard. For susceptor microwave applications, we apply the CF of 0.001 that FDA has established for these materials. See **Attachment 20** for these calculations.

For each component, the two separate dietary concentrations calculated for Conditions of Use B-H and microwave susceptors may be summed to calculate the total dietary concentration. The total values thus calculated are shown in Section II.G.3 below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
FCS Oligomers	--	See Attachment 18	0.28	0.00084	
2-Perfluorohexylethyl methacrylate	2144-53-8	--	(b) (4)		
Diethylaminoethyl methacrylate	105-16-8	--			
Methacrylic acid	79-41-4	--			
Acrylic acid	79-10-7	--			
(b) (4)		--			
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: May 14, 2009

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 885:** Keller and Heckman LLP (K&H) on behalf of DuPont Chemical Solutions Enterprise (DuPont). Use of a perfluoroalkylethyl methacrylate copolymer as an oil and grease resistant treatment for paper and paperboard employed either prior to the sheet forming operation or at the size press. Submissions received February 9, 2009 (initial submission) and April 23, 2009 (response to environmental deficiencies).

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 1
Attention: P. Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of DuPont Chemical Solutions Enterprise (DuPont), submitted this food contact notification (FCN) for the use of a perfluoroalkylethyl methacrylate copolymer as an oil and grease resistant treatment for paper and paperboard, at a level not to exceed 0.42 weight percent (wt.-%), employed either prior to the sheet forming operation (aka wet-end) or at the size press. Paper manufactured from the food contact substance (FCS) may be used under Conditions of Use B through H and J (microwave susceptor applications). The commercial product, marketed as (b) (4), consists of an aqueous dispersion containing approximately 19.5% solids.

Background

The FCS is not currently regulated under 21 CFR 170-199 nor is it the subject of any effective FCNs. There are numerous perfluoro-based grease-proofing agents regulated or otherwise authorized for use in contact with food. The FCSs identified in DuPont's FCNs (b) (4) [1] (effective June 12, 2002), (b) (4) [2] (effective April 15, 2003), (b) (4) [3] (effective August 19, 2003), and (b) (4) [4] (effective September 30, 2006), marketed as (b) (4) products, are prepared from similar perfluoroalkylethyl acrylate monomers, for use under Conditions B through H and J (microwave susceptor). The subject FCS differs in that the (b) (4)

Chemistry information is contained in FDA Form 3480 and Attachments 1 (structural formula and composition), 2 (molecular weight distribution data), 3 (infrared and nuclear magnetic resonance

[1] Chemistry memorandum for (b) (4) dated June 10, 2002 (K. Arvidson to J. Smith).
[2] Chemistry memoranda for (b) (4) 1 dated February 20, 2003 and December 8, 2003 (K. Smeds to K. Williams).
[3] Memorandum to the file for (b) (4) dated May 30, 2003 (K. Randolph).
[4] Chemistry memorandum for (b) (4) dated September 26, 2006 (K. Paquette to P. Honigfort).

spectra), 4 (manufacturing process), 5 (residual impurity levels), 6 (determination of (b) (4) diethylaminoethyl methacrylate, (b) (4) , and (b) (4) l by gas chromatography with a flame ionization detector, GC-FID), 7 (determination of acrylic acid and methacrylic acid by GC-FlD), 8 (determination of residual telomer intermediates by GC/MS), 9 (determination of several residual (b) (4) by liquid chromatography, LC/MS/MS), 10 (determination of (b) (4) by GC-FID), 11 (determination of (b) (4) by GC), 12 (FCS specifications), 13 (test methods for physical properties), 15 (technical information), 16 (thermogravimetric analysis), 17 (exhaustive extraction study), 18 (migration calculations), 19 (comparison of the FCS with (b) (4)), and 20 (exposure estimates). The suggested language for the FCS and proposed use is provided in Attachment 14.

Identity

Information on the identity of the FCS is contained in Form 3480, Sections II.A. and II.C., and Attachments 1-3 and 12-13.

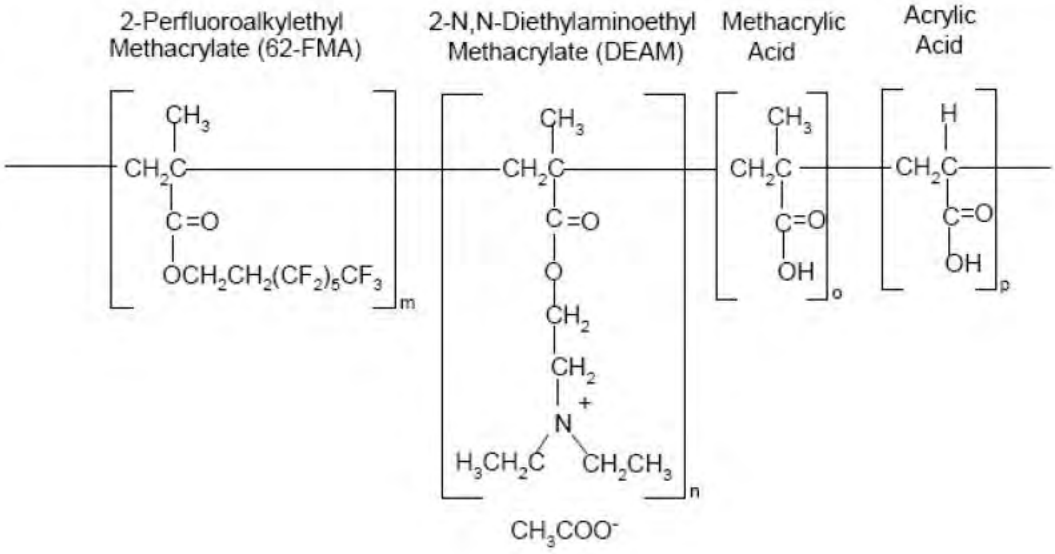
The FCS is a fluoropolymer based on a methacrylate backbone with pendant (perfluorohexyl)ethyl (from 2-perfluorohexylethyl methacrylate, 62-FMA) and diethylaminoethyl (from diethylaminoethyl methacrylate, DEAM) groups. As indicated in Section II.A.5, the commercial product consists of an aqueous dispersion containing approximately 19.5% solids.

CAS name: 2-propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2 propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate.

CAS Reg. No.: 1071022-26-8

Other names: (b) (4)
Acetate salts of methacrylic acid copolymer with acrylic acid, diethylaminoethyl methacrylate, and 2-(perfluorohexyl)ethyl methacrylate.

Structure: The structure of the FCS, as taken from Attachment 1, is shown below.



(b) (4) [redacted]

Specifications: Specifications for the commercial product (MW, appearance, solid content, density, pH, flash point and viscosity) were provided in Section II.C and Attachment 12. Attachment 13 contains test methods for determining the specifications. An MSDS for the commercial product is provided in Attachment 15.

Characterization: The notifier provided infrared and nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra in Attachment 3.

Molecular weight distribution (MWD)

Attachment 2 contains gel permeation chromatography (GPC) data for three batches of the commercial product. The attachment also details the ethanol extraction carried out on the dried solids in an effort to obtain a more accurate representation of the fraction of oligomers <2000 D in the polymer.

Number average molecular weight (M_n) = (b) (4) [redacted]
Weight average molecular weight (M_W) = (b) (4) [redacted]
Fraction of oligomers <2000 D = 0.045 wt.-%

Ethanol extraction for total non-volatile extractives (TNEs)

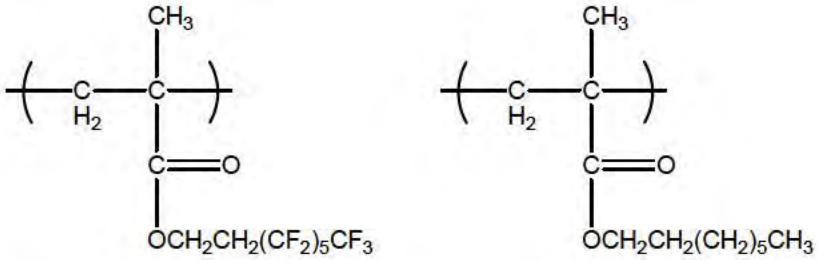
402 g Capstone P-620 active solid, corresponding to a 2000 g commercial solution (19.5% solids), was added to a round bottom flask equipped with a condenser. 95% Ethanol (1000 g) was added and the mixture was heated to 55°C for 1 hour. The ethanol solution was decanted and the remaining (b) (4) [redacted] was washed with ethanol (20 g). The combined liquor was air dried yielding 4.08 g (1.01wt. %) of a yellow/orange solid. We will refer to this as TNEs in this memorandum

GPC Analysis of TNEs

Analysis of the TNEs indicated that 6 wt.-% consisted of oligomers with a MW <2000 D. The notifier noted that for the approximately 1% TNEs obtained by ethanol extraction, a minimum of about 25% was attributable to identifiable impurities as analyzed by GC, including residual monomers and dispersant. Therefore, an upper limit of the extracted fluoropolymer is about 75% of the 1%, or 0.75%. Thus, the 6% fluoropolymer with a MW<2000 D corresponds to a maximum of 0.045% (or 0.76% x 6%) of the total fluoropolymer in the commercial product.

We would like to note that for the FCS, Toxicology typically requests that we calculate exposure to the fraction of oligomers <1000 Daltons. In reviewing the chemistry memoranda for various FCNs for other perfluorinated grease-proofing agents, we have previously provided toxicology with exposure values based on the MW fractions with <1000, 2200 and 2500 D. In addition, there have

been a number of discussions regarding the relative size of these perfluorinated oligomers versus their hydrocarbon analogs and how that might affect absorption in the gut. While chemistry cannot speak to the bioavailability of these perfluorinated species compared to their hydrocarbon analogs, we can provide some insight into their relative size. Using Chem3D Ultra[5] version 6.0, we have determined the solvent-excluded volume and MW of a representative repeat unit in the FCS and the analogous hydrocarbon version of that same repeat unit.



The repeat unit containing the fluorinated side chain (depicted above on the left) had a MW of 432 D and a solvent excluded volume of 245 cubic Ångstroms while the hydrocarbon analog (depicted above on the right) had a MW of 198 Daltons and a solvent excluded volume of 208 cubic Ångstroms. From these data, there appears to be very little difference in the actual volume (size) of the fluorine-containing repeat unit and the hydrocarbon repeat unit (a factor of 1.18), whereas there is a factor of 2.18 difference in the MWs of these repeat units. To normalize the MW cutoff for exposure estimates of perfluorinated oligomers from this FCS with the hydrocarbon analogs we will apply a correction factor of 2.18, which gives a MW cutoff of 2100 D (versus the 1000 D cutoff typically used by our toxicologists) for perfluoro oligomers. The notifier used a cutoff of 2000 D which is sufficient for the subject FCS.

We have no questions on the identity of the FCS.

Manufacture

Manufacturing information is contained in Form 3480, Section II.B, and Attachments 4-11. Raw materials used to manufacture the FCS are listed in Section II.B.1, and summarized in Table 1, below. A description of the manufacturing process is provided in Attachment 4. The process is very similar to that used in the manufacture of (b) (4) products.

(b) (4)

In Attachment 4, the notifier notes that the manufacturing process for the FCS has been adjusted to

[5] CambridgeSoft Corp., Cambridge, MA 02140.

increase the MW of the finished polymer. These modifications involve some slight adjustments in the relative ratios of some of the process chemicals as outlined in Attachment 4.

Table 1: Raw materials used to manufacture the FCS

Material	CAS Reg. No.	Function	Relative Conc.
2-Perfluorohexylethyl methacrylate (62-FMA)	2144-53-8	Monomer	(b) (4)
diethylaminoethyl methacrylate (DEAM)	105-16-8	Monomer	
Methacrylic acid (MAA)	79-41-4	Monomer	
Acrylic acid (AA)	79-10-7	Monomer	
(b) (4)			

Impurities

In Section II.B.3, the notifier identified 10 impurities in the commercial product (containing ~19.5% polymer solids) and provided maximum levels for 6 of those impurities. In Attachment 5, the notifier provided impurity levels measured in three representative lots of the commercial product. The table in Attachment 5 of the FCN is included as Appendix 1 to this memorandum. The averaged residue levels for some of the impurities (exception being those that were analyzed from paper extracts as described below) are summarized below in Table 2 (column 2). The analytical reports, including the test methods, are provided in Attachments 6-11 as described below.

We note that (b) (4) was identified as an impurity. (b) (4) is produced from the decomposition of the (b) (4) during the polymerization procedure. (b) (4) is regulated for use as a polymerization catalyst in 21 CFR 176.170 (Components of paper and paperboard in contact with aqueous and fatty foods), and therefore, no exposure calculation for (b) (4) is necessary.

Attachment 6: Determination of (b) (4) DEAM, (b) (4) , and (b) (4) by GC-FID[6]

[6] We note that the analysis was carried out on the commercial product that is the subject of this FCN as well as other products marketed by the notifier. Furthermore, the notifier did not explicitly provide the amount of sample used in the analysis. Nonetheless, the analytical report is adequate.

This method was based on extraction of the sample with acetonitrile (ACN) followed by filtration and GC analysis on a deactivated fused silica capillary column coated with Rtx-5 Amine (5% diphenyl/95% dimethylpolysiloxane). The separated components were detected by FID.

DEAM momomer and three decomposition products, (b) (4) and telomer B alcohol (from 62-FMA) were quantified on a weight percent basis using an external standard calibration. Telomer B alcohols included (b) (4)

Calibration Standards

(b) (4) calibration standards (0.05, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of (b) (4) (0.031 g (b) (4) diluted with ACN in a 25 mL volumetric flask) with ACN.

DEAM and (b) (4) calibration standards (0.005, 0.5, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.031 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

(b) (4) calibration standards (0.08, 0.40, and 0.80 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.05 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

(b) (4) calibration standards (0.05, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.05 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

Sampling and analysis

(b) (4) was weighed and placed in a vial. ACN (10 mL) was added and the contents sonicated. The ACN extract was filtered, transferred to a GC vial and sealed. An aliquot of the sample solution was injected into the GC and analyzed. The method was adequately validated. Two sets of data (from one plant batch and two pilot batches, and validation studies) were provided in Attachment 6.

Attachment 7: Determination of AA and MAA by GC-FID

This method was based on extraction of the sample with ACN followed by filtration and analysis by GC on an HP-5 capillary column fused silica coated with 5% phenylmethylsiloxane. The separated components were detected by FID.

Calibration Standards

AA and MAA calibration standards (100, 500 and 1000 ppm) were prepared by diluting a 10,000 ppm stock solution of the appropriate impurity with ACN.

Sampling and analysis

(b) (4) (2 g) was weighed and placed in a vial. ACN (10 mL) was added to the vial which was then sonicated. An aliquot was then transferred into a GC vial and analyzed. The method was adequately validated.

Attachment 8: Determination of residual telomer intermediates by GC/MS

This method determined the concentration of residual telomer intermediates in the FCS including:

- homologues of Telomer A: C6-I (perfluorohexyliodide), C8-I (perfluorooctyliodide), and C10-I (perfluorodecyliodide).

- homologues of Telomer B: C6 (6-2I; 1H,1H,2H,2H-perfluorooctyl iodide), C8 (8-2I; 1H,1H,2H,2H-perfluorodecyl iodide), and C10 (10-2I; 1H,1H,2H,2H-perfluorododecyl iodide).

- homologues of Telomer BA: C6 (6-2A; 1H,1H,2H,2H-perfluorooctan-1-ol), C8 (8-2A; 1H,1H,2H,2H-perfluorodecan-1-ol), C10 (10-2A; 1H,1H,2H,2H-perfluorododecan-1-ol).

- C8 Olefin (1H,1H,2H-perfluoro-1-decene).

- 8-2-8 Ester (2-(perfluorooctyl)ethylperfluorooctanoate).

Calibration Standards
Calibration standards of the telomer intermediates (0.1, 0.5, 1, 5, 10, and 20 ppm) were prepared by diluting a 20 ppm stock solution of the appropriate impurity with ACN.

Sampling and analysis
(b) (4) (200 mg) was weighed and placed in a vial. ACN (5 mL) was added, the contents sonicated, then transferred to a vial and analyzed by GC/MS. The method was adequately validated.

Attachment 9: Determination of residual (b) (4) by LC/MS/MS

This method determined the concentration of residual (b) (4)

Based on the manufacturing process of the FCS, which involved C6 chemistry, we would not expect significant levels of the other (b) (4) to be present in the FCS.

Calibration Standards

Calibration standards of residual (b) (4) (0.5, 1, 10, 25, 50 and 100 ppb) were prepared by diluting a stock solution of the appropriate PFCA with methanol.

Sampling and analysis
Samples (60 mg) were weighed and placed into 20 mL scintillation vials. Water was added and the samples were filtered, as needed. Sample (250 uL), water (250 uL), and internal standard (500 uL of a 50 ppb internal standard) were placed in an LC vial, and analyzed. The method was adequately validated.

Attachment 10: Determination of (b) (4) by GC-FID

This method was based on extraction of the sample with ACN followed by filtration and analysis by GC on a DB-1701 capillary column, crosslinked and surface bonded with 14% cyanopropylphenyl/ 85% dimethylpolysiloxane. The separated components were detected by FID.

Calibration Standards
Calibration standards of (b) (4) (50, 100, 500 and 1000 mg/L) were prepared by diluting a 10,000 mg/L stock solution of the appropriate impurity with ACN.

Sampling and analysis
(b) (4) (2 g) was weighed and placed in a vial. N,N-Dimethylacetamide, DMAC (10 mL) was added to the vial which was then sonicated. An aliquot was then transferred into a GC vial and analyzed. The method was adequately validated.

Attachment 11: Determination of (b) (4) by GC-FID[6]

This method was based on analysis of a sample (identified as (b) (4)) in tetrahydrofuran (THF) by GC on a fused-silica capillary column coated with a free fatty acid phase. The separated components were detected by FID.

Calibration Standards
A calibration standard of (b) (4) (200 ppm) was prepared by diluting a stock solution of (b) (4) with THF.

Sampling and analysis
(b) (4) was weighed and placed in a vial. THF (10 mL) was added to a vial which was then shaken. An aliquot was then transferred into a GC vial and analyzed by GC-FID. The method was adequately validated.

As noted above, impurities and residual levels in three batches of the commercial product are summarized in Appendix 1 to this memorandum. The average values for some of these impurities, as taken from Attachments 5 and 18, are shown in Table 2, below.

Table 2: Summary of Impurity Levels in the Commercial Product (19.5% solids)

Substance	Avg. Residual levels in commercial product
Monomers and LMWOs	
62-FMA	89 ppm (0.1% max)[a,b]
DEAM	100 ppm (0.03% max)[a]
MAA	<50 ppm
AA	<50 ppm
LMWOs	[c]
By-products	

(b) (4)

PFCAs and related substances

(b) (4)

[a] Maximum residual levels were taken from FDA Form 3480, Section II.B.3.
[b] Exposure to these impurities will be based on results of the exhaustive extraction described in the Migrant Levels in Food section below, rather than the residual levels reported in this table.
[c] Based on a LMWO fraction <2000 D of 0.045 wt.-%.
[d] (b) (4) All other (b) (4) and (b) (4) s were non-detected or below the limit of quantitation in all samples analyzed.

We have no questions on the manufacture of and impurities in the FCS.

Intended Use and Technical Effect

Information on the intended use and technical effect of the FCS is contained in Section II.D. of Form 3480, and Attachments 14-15.

The FCS is intended to be used as an oil and grease resistant treatment for paper and paperboard employed either prior to the sheet forming operation (aka wet-end) or at the size press. The FCS may be used at a level not to exceed 0.42 wt.-% of dry paper and paperboard intended for use in contact with all food types under Conditions of Use B through H and J (microwave susceptor applications). The proposed use is substitutional for the uses notified in DuPont's FCNs (b) (4) (b) (4). As indicated in Attachment 18, the subject FCS is intended to replace the FCSs that are the subject of FCNs (b) (4).

In Section II.D.3, the notifier indicated that the utility of the FCS as an oil and grease resistant treatment was measured using established paper industry performance test procedures. The grease resistance test (TAPPI test method T 559 pm-96) was performed on treated and untreated paper sheets to demonstrate performance efficacy of the commercial product. This procedure was also used in FCN (b) (4).

A base paper sheet (38 lb) was treated with a sizing solution (b) (4) and 2% of (b) (4) (containing ~19.5% polymer solids, therefore, the paper was treated at a maximum level corresponding to 0.42 wt.-% polymer solids on the paper) at (b) (4). The treated paper sheet was subsequently dried by a laboratory drum drier (b) (4). The dried paper contained (b) (4) fluorine. The treated paper sheet exhibited a repellency rating of 12, indicative of a high degree of grease repellency. The untreated base paper sheet exhibited a rating of less than 1. The notifier noted that these results clearly demonstrate the technical effect of the FCS as a grease resistance agent.

A technical information sheet for the commercial product is provided in Attachment 15. The suggested language for the FCN is contained in Attachment 14. We concur with this language.

We have no questions on the intended use and technical effect of the FCS.

Stability

In Form 3480, Section II.E., the notifier stated that, as indicated in the manufacturing process description in Attachment 4, a very small amount of hydrolysis of the polymer side chains may occur during post-polymerization, resulting in the formation of minor amounts of (b) (4) as by-products of the acrylate monomers DEAM and 62-FMA, respectively.

The notifier noted that the thermal stability of the FCS was evaluated by thermogravimetric analysis (TGA) of the FCS from 0 to 235°C. The thermal stability of the FCS was also evaluated by NMR spectroscopic comparison of the dried polymer before and after exposure to high temperatures to simulate the proposed conditions of use (see Attachment 16). The TGA showed a weight loss of (b) (4) Analysis by ^{13}C NMR before and after heating to 235°C did not indicate any change in the polymer structure.

We have no questions regarding the stability of the FCS under its intended conditions of use.

Migrant Levels in Food

The notifier did not carry out migration studies to support the proposed use. Rather, in Form 3480, Section II.F, the notifier calculated the worse-case migration of FCS oligomers and impurities based on measured levels in the commercial product or from extraction studies conducted on paper manufactured from the FCS are described below.

Attachment 17 contains the results of exhaustive extractions of paper manufactured with the FCS using chloroform ($CHCl_3$) as the extraction solvent. The extracts were analyzed for 62-FMA, (b) (4) and (b) (4). 62-FMA, (b) (4) and (b) (4) calibration standards (50, 100 and 1000 ng/mL) were prepared by diluting a 1000 µg/mL stock solution of the appropriate impurity with $CHCl_3$.

Paper samples (two 8.5"x11" sheets, 59 g/m^2) treated at the size press with the FCS (0.42% by weight) were Soxhlet extracted with $CHCl_3$ (56.7 mL) for 6 hours and the resulting extracts analyzed by GC/MS for impurities. The same paper samples were extracted a second time for 4 hours with fresh $CHCl_3$ (56.7 mL). The average level of 62-FMA was 84 ng/mL (or 0.0255 µg/in^2 paper sample), (b) (4) The method was adequately validated. Results are presented in Table 2, above.

Consumer Exposure

Information on consumer exposure is contained in Form 3480, Section II.G, and Attachments 18-20. The notifier used the results of the GPC analysis of TNEs, the residue levels determined by direct analysis of the commercial product (Table 2, column 2), and extraction of paper manufactured from the FCS, to determine migration to food. Exposure estimates are provided in

Table 3, below.

Low molecular weight oligomers (LMWOs)

In Attachment 18, the notifier calculated the worst-case migration, <M>, of LMWOs based on a MW <2000 D (0.045 wt.-%), and the maximum FCS use level (0.42% on the polymer solids basis). For Conditions of Use B through H, the notifier assumed a typical food-contact paper basis weight of 0.05 g/in^2 (50 mg/in^2) and our default food mass-to-surface area ratio of 10 g food/in^2. For use condition J, the notifier assumed a paper basis weight of 0.023 g/in^2 (a typical paper weight for microwave susceptors applications), and a food ratio of 5 g/in^2 as follows:

$<M>_{Oligomers,\ B\text{-}H}$ =
= (0.00045 g oligmers/g FCS)(0.0042 g FCS/g paper)(0.05 g paper/in^2)(1 in^2/10 g food)
= 9.5×10^{-9} g oligomers/g food or 9.5 ppb

$<M>_{Oligomers,\ J}$ =
= (0.00045 g oligmers/g FCS)(0.0042 g FCS/g paper)(0.023 g paper/in^2)(1 in^2/5 g food)
= 8.7×10^{-9} g oligomers/g food or 8.7 ppb

The notifier then indicated that migration data previously submitted for the closely related polymer that was the subject of FCNs (b) (4) (a copolymer of a 2-perfluoroalkylethyl acrylate with a range of $(CF_2)_n$ groups where n=(b) (4), DEAM and glycidyl methacrylate, marketed as (b) (4) product) demonstrated that only a portion of the oligomers present migrate to 10% ethanol when tested under Condition of Use B. Specifically, the migration studies described in FCN (b) (4) were conducted on paper samples (basis weight 0.036 g/in^2) containing 0.33% of polymer. The oligomer content of the FCS in FCN (b) (4) was 0.84%, and testing resulted in 25 ppb migration of oligomers to 10% ethanol.

Assuming that 100% of the available oligomers migrated to food, the worst-case migration for the samples tested would be 100 ppb or (0.0084 g oligomers/g FCS)x(0.0033 g FCS/g paper)x(0.036 g paper/in^2)x(1 in^2/10 g food). Thus, the actual measured migration of 25 ppb represents a ¼ (or 25%) of the migration of the oligomer content of the polymer in FCN (b) (4). The notifier applied this rationale to the present FCN to determine a migration of oligomers (from the subject FCN) to aqueous food, under Conditions of Use B, of 2.4 ppb as follows.

$<M>_{Oligomers,\ B\text{-}H,\ aqueous\ foods}$ = 9.5 ppb x 25% = 2.4 ppb

In Attachment 20, the notifier used the <M> values calculated above, the applicable CFs (0.05 for specialty paper and 0.001 for microwave susceptor applications), and food-type distribution factors (for Conditions of Use B through H) to estimate a dietary concentration (DC) as follows:

$DC_{B\text{-}H} = CF_{specialty\ paper} \times <M>_{B\text{-}H} = 0.05 \times [(2.4\ ppb \times 0.59) + (9.5\ ppb \times 0.41)]$
$= 0.05 \times 5.3\ ppb = 0.27\ ppb$

$DC_J = CF_{microwave\ susceptor} \times <M>_J = 0.001 \times 8.7\ ppb = 0.009\ ppb$

$DC_{Total} = DC_{B-H} + DC_J = 0.27$ ppb + 0.009 ppb = 0.28 ppb

62-FMA, (b) (4) (exhaustive extraction)

For the impurities determined in the exhaustive extraction described in Section II.F, the notifier calculated migration levels to food based on the extracted levels from the treated paper samples (basis weight of 59 g/m^2 or 0.038 g/in^2). The notifier first applied a correction factor to the measured levels of the three analytes to account for differences in the paper basis weight (0.05 g/in^2 for condition B through H and 0.023 g/in^2 for condition J) as follows:

$\langle M \rangle_{62\text{-}FMA,B\text{-}H}$: (0.0255µg/in^2)(0.05 g/in^2 ÷ 0.038 g/in^2)(in^2/10 g food) = 0.00336 µg/g = 3.4 ppb

(b) (4)

The <M> for (b) (4) for conditions B through H, and J, respectively, and <M> for (b) (4) for conditions B through H, and J, respectively.

The notifier then used the <M> values and the applicable CFs to estimate exposure.

DEAM

In Attachment 18, the notifier indicated that DEAM was used as a monomer in the closely related polymer that was the subject of DuPont's FCNs (b) (4) and that the maximum residual specification for DEAM in the finished product in the subject FCN is identical to that in the previous notifications. The notifier indicated that in FCN (b) (4), the DC for DEAM was (b) (4) This exposure was based on the results of migration testing conducted under condition of use B. The FCS in FCN (b) (4) is used at levels up to 0.69%, whereas the subject FCS is limited to a maximum of 0.42%. Therefore, the previously calculated exposure can be adjusted by a factor of 0.61 (or 0.42/0.69) to calculate a DC for DEAM from the subject FCN. The DC for DEAM, under Conditions B through H, would be 0.085 ppb (or 0.61 x 0.14 ppb).

For use in microwave susceptor applications, the notifier calculated a DC assuming 100% migration, as described below.

Other impurities

For the remaining impurities that may be present in the commercial product, the notifier estimated exposure based on the average concentrations measured in the commercial product containing 19.5% polymer solids (shown in Table 2 above). The notifier first converted the concentrations in the commercial product to concentrations in the polymer solid (by dividing by a factor of 0.195). The notifier then used the maximum FCS use level (0.42% on the polymer solids basis) and the applicable paper basis weight, food mass-to-surface area ratio and CF to estimate exposure. Exposure estimates are provided in Table 3, below. We concur with the notifier's approach and

with the notifier's exposure estimates.

Table 3: Exposure estimates

Substance	$<M>_{B-H}$ (ppb)	$<M>_{J}$ (ppb)	DC_{B-H} (ppb)	DC_{J} (ppb)	DC_{Total} (ppb)
Monomers and LMWOs					
62-FMA	(b) (4)				
DEAM					
MAA					
AA					
LMWOs	5.3[c]	8.7[c]	0.27	0.009	0.28
By-products					
(b) (4)					
PFCAs and related substances					
(b) (4)					

(b) (4)

[a] Based on the results of the exhaustive extraction described in the Migrant Levels in Food section.
[b] Based on the discussion presented in the Exposure section.
[c] Based on a LMWO fraction <2000 D of 0.045 wt.-%.
[d] As indicated in the impurity section above, (b) (4) is produced from the decomposition of the (b) (4) during the polymerization procedure. Since (b) (4) is regulated for use as a polymerization catalyst in §CFR 176.170, no exposure calculation for TMSN is necessary.

We have no questions on consumer exposure.

Notification Language

The acknowledgment letter, signed off by Chemistry on May 6, 2009, is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb: FCN885_C_memo
RDInit: ABBailey, 5-12-09
Final: seb, 5-14-09

Appendix

(C10-2A)					
Perfluorooctyl ethylene (C8 olefin)	<0.215	<0.20	<0.011	<0.0002	<0.011
2-(Perfluorooctyl)ethylper-fluorooctanoate (8-2-8 ester)	<0.215	<0.20	<0.011	<0.0002	<0.011
Solvents					
MIBK	Essentially zero				
IPA	Essentially zero				

[a] Based on the results of the exhaustive extraction described in the Migrant Levels in Food section.
[b] Based on the discussion presented in the Exposure section.
[c] Based on a LMWO fraction <2000 D of 0.045 wt.-%.
[d] As indicated in the impurity section above, TMSN is produced from the decomposition of the AIBN during the polymerization procedure. Since AIBN is regulated for use as a polymerization catalyst in §CFR 176.170, no exposure calculation for TMSN is necessary.

We have no questions on consumer exposure.

Notification Language

The acknowledgment letter, signed off by Chemistry on May 6, 2009, is appropriate as written.

Conclusion

We have no questions on this FCN.

(b) (6)

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb: FCN885_C_memo
RDInit: ABBailey, 5-12-09
Final: seb, 5-14-09

Appendix

Appendix 1- Summary of Residue Results From Attachment 5 of FCN 885

Analyte	Synonym	Attachment No.	Plant Batch 2	Pilot Batch 4	Pilot Batch 5
(b) (4)					
Perfluorohexylethyl methacrylate	62-FMA	6	(b) (4)		
(b) (4)					
2-(Diethylamino)ethyl methacrylate	DEAM	6	(b) (4)		
(b) (4)					
Methacrylic acid	MA	7	(b) (4)		
Acrylic acid	AA	7			
(b) (4)					

Memorandum

Date: May 14, 2009

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 885:** Keller and Heckman LLP (K&H) on behalf of DuPont Chemical Solutions Enterprise (DuPont). Use of a perfluoroalkylethyl methacrylate copolymer as an oil and grease resistant treatment for paper and paperboard employed either prior to the sheet forming operation or at the size press. Submissions received February 9, 2009 (initial submission) and April 23, 2009 (response to environmental deficiencies).

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 1
Attention: P. Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of DuPont Chemical Solutions Enterprise (DuPont), submitted this food contact notification (FCN) for the use of a perfluoroalkylethyl methacrylate copolymer as an oil and grease resistant treatment for paper and paperboard, at a level not to exceed 0.42 weight percent (wt.-%), employed either prior to the sheet forming operation (aka wet-end) or at the size press. Paper manufactured from the food contact substance (FCS) may be used under Conditions of Use B through H and J (microwave susceptor applications). The commercial product, marketed as (b)(4), consists of an aqueous dispersion containing approximately 19.5% solids.

Background

The FCS is not currently regulated under 21 CFR 170-199 nor is it the subject of any effective FCNs. There are numerous perfluoro-based grease-proofing agents regulated or otherwise authorized for use in contact with food. The FCSs identified in DuPont's FCNs 206[1] (effective June 12, 2002), 311[2] (effective April 15, 2003), 338[3] (effective August 19, 2003), and 646[4] (effective September 30, 2006), marketed as (b)(4), are prepared from similar perfluoroalkylethyl acrylate monomers, for use under Conditions B through H and J (microwave susceptor). The subject FCS differs in that the pendant perfluoro groups are based on a single fluorinated alcohol, $(CF2)_6CH_2CH_2OH$, rather than a range of fluorinated alcohols as is the case for the (b)(4)

Chemistry information is contained in FDA Form 3480 and Attachments 1 (structural formula and composition), 2 (molecular weight distribution data), 3 (infrared and nuclear magnetic resonance

[1] Chemistry memorandum for FCN 206 dated June 10, 2002 (K. Arvidson to J. Smith).
[2] Chemistry memoranda for FCN 311 dated February 20, 2003 and December 8, 2003 (K. Smeds to K. Williams).
[3] Memorandum to the file for FCN 338 dated May 30, 2003 (K. Randolph).
[4] Chemistry memorandum for FCN 646 dated September 26, 2006 (K. Paquette to P. Honigfort).

spectra), 4 (manufacturing process), 5 (residual impurity levels), 6 (determination of diethylaminoethanol, diethylaminoethyl methacrylate, tetramethyl butyrodinitrile, and Telomer B alcohol by gas chromatography with a flame ionization detector, GC-FID), 7 (determination of acrylic acid and methacrylic acid by GC-FlD), 8 (determination of residual telomer intermediates by GC/MS), 9 (determination of several residual perfluorocarboxylic acids by liquid chromatography, LC/MS/MS), 10 (determination of 2-propanol and 4-methyl-2-pentanone by GC-FID), 11 (determination of hydroquinone monomethyl ether by GC), 12 (FCS specifications), 13 (test methods for physical properties), 15 (technical information), 16 (thermogravimetric analysis), 17 (exhaustive extraction study), 18 (migration calculations), 19 (comparison of the FCS with Zonyl 9464), and 20 (exposure estimates). The suggested language for the FCS and proposed use is provided in Attachment 14.

Identity

Information on the identity of the FCS is contained in Form 3480, Sections II.A. and II.C., and Attachments 1-3 and 12-13.

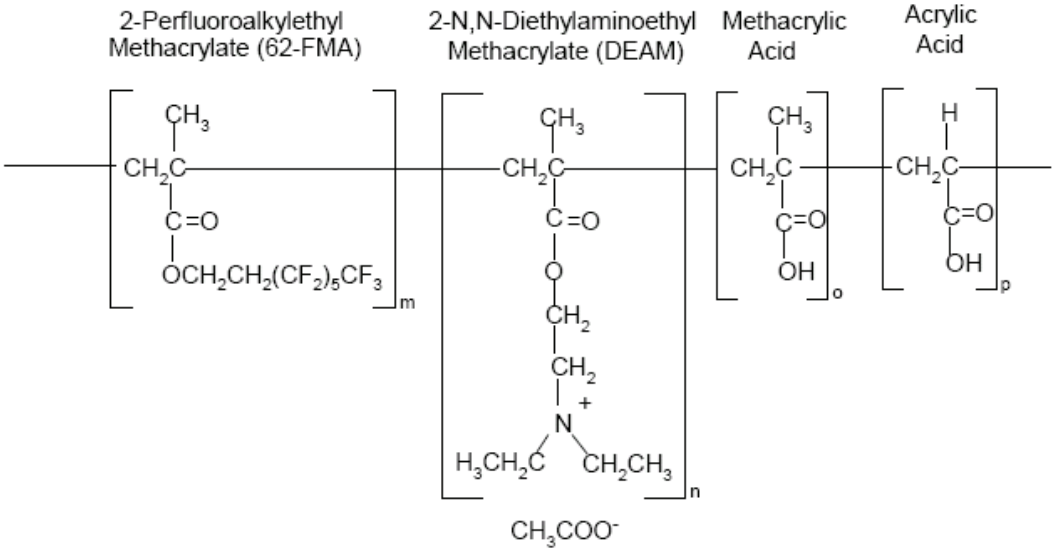
The FCS is a fluoropolymer based on a methacrylate backbone with pendant (perfluorohexyl)ethyl (from 2-perfluorohexylethyl methacrylate, 62-FMA) and diethylaminoethyl (from diethylaminoethyl methacrylate, DEAM) groups. As indicated in Section II.A.5, the commercial product consists of an aqueous dispersion containing approximately 19.5% solids.

CAS name: 2-propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2 propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate.

CAS Reg. No.: 1071022-26-8

Other names: (b)(4)
Acetate salts of methacrylic acid copolymer with acrylic acid, diethylaminoethyl methacrylate, and 2-(perfluorohexyl)ethyl methacrylate.

Structure: The structure of the FCS, as taken from Attachment 1, is shown below.



(b)(4)

Specifications: Specifications for the commercial product (MW, appearance, solid content, density, pH, flash point and viscosity) were provided in Section II.C and Attachment 12. Attachment 13 contains test methods for determining the specifications. An MSDS for the commercial product is provided in Attachment 15.

Characterization: The notifier provided infrared and nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra in Attachment 3.

Molecular weight distribution (MWD)

Attachment 2 contains gel permeation chromatography (GPC) data for three batches of the commercial product. The attachment also details the ethanol extraction carried out on the dried solids in an effort to obtain a more accurate representation of the fraction of oligomers <2000 D in the polymer.

Number average molecular weight (M_n) = (b)(4)
Weight average molecular weight (M_W) = (b)(4)
Fraction of oligomers <2000 D = 0.045 wt.-%

Ethanol extraction for total non-volatile extractives (TNEs)

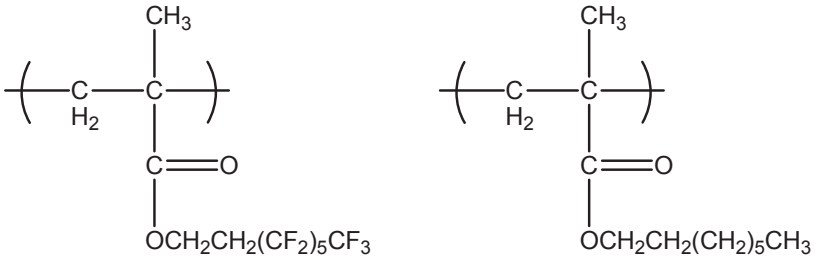
402 g (b)(4) active solid, corresponding to a 2000 g commercial solution (19.5% solids), was added to a round bottom flask equipped with a condenser. 95% Ethanol (1000 g) was added and the mixture was heated to 55°C for 1 hour. The ethanol solution was decanted and the remaining (b)(4) solid was washed with ethanol (20 g). The combined liquor was air dried yielding 4.08 g (1.01wt. %) of a yellow/orange solid. We will refer to this as TNEs in this memorandum

GPC Analysis of TNEs

Analysis of the TNEs indicated that 6 wt.-% consisted of oligomers with a MW <2000 D. The notifier noted that for the approximately 1% TNEs obtained by ethanol extraction, a minimum of about 25% was attributable to identifiable impurities as analyzed by GC, including residual monomers and dispersant. Therefore, an upper limit of the extracted fluoropolymer is about 75% of the 1%, or 0.75%. Thus, the 6% fluoropolymer with a MW<2000 D corresponds to a maximum of 0.045% (or 0.76% x 6%) of the total fluoropolymer in the commercial product.

We would like to note that for the FCS, Toxicology typically requests that we calculate exposure to the fraction of oligomers <1000 Daltons. In reviewing the chemistry memoranda for various FCNs for other perfluorinated grease-proofing agents, we have previously provided toxicology with exposure values based on the MW fractions with <1000, 2200 and 2500 D. In addition, there have

been a number of discussions regarding the relative size of these perfluorinated oligomers versus their hydrocarbon analogs and how that might affect absorption in the gut. While chemistry cannot speak to the bioavailability of these perfluorinated species compared to their hydrocarbon analogs, we can provide some insight into their relative size. Using Chem3D Ultra[5] version 6.0, we have determined the solvent-excluded volume and MW of a representative repeat unit in the FCS and the analogous hydrocarbon version of that same repeat unit.



The repeat unit containing the fluorinated side chain (depicted above on the left) had a MW of 432 D and a solvent excluded volume of 245 cubic Ångstroms while the hydrocarbon analog (depicted above on the right) had a MW of 198 Daltons and a solvent excluded volume of 208 cubic Ångstroms. From these data, there appears to be very little difference in the actual volume (size) of the fluorine-containing repeat unit and the hydrocarbon repeat unit (a factor of 1.18), whereas there is a factor of 2.18 difference in the MWs of these repeat units. To normalize the MW cutoff for exposure estimates of perfluorinated oligomers from this FCS with the hydrocarbon analogs we will apply a correction factor of 2.18, which gives a MW cutoff of 2100 D (versus the 1000 D cutoff typically used by our toxicologists) for perfluoro oligomers. The notifier used a cutoff of 2000 D which is sufficient for the subject FCS.

We have no questions on the identity of the FCS.

Manufacture

Manufacturing information is contained in Form 3480, Section II.B, and Attachments 4-11. Raw materials used to manufacture the FCS are listed in Section II.B.1, and summarized in Table 1, below. A description of the manufacturing process is provided in Attachment 4. The process is very similar to that used in the manufacture of DuPont's (b)(4)

(b)(4)

In Attachment 4, the notifier notes that the manufacturing process for the FCS has been adjusted to

[5] CambridgeSoft Corp., Cambridge, MA 02140.

increase the MW of the finished polymer. These modifications involve some slight adjustments in the relative ratios of some of the process chemicals as outlined in Attachment 4.

Table 1: Raw materials used to manufacture the FCS

Material	CAS Reg. No.	Function	Relative Conc.
2-Perfluorohexylethyl methacrylate (62-FMA)	2144-53-8	Monomer	38.85
diethylaminoethyl methacrylate (DEAM)	105-16-8	Monomer	9.26
Methacrylic acid (MAA)	79-41-4	Monomer	1.16
Acrylic acid (AA)	79-10-7	Monomer	1.16
(b)(4)			

Impurities

In Section II.B.3, the notifier identified 10 impurities in the commercial product (containing ~19.5% polymer solids) and provided maximum levels for 6 of those impurities. In Attachment 5, the notifier provided impurity levels measured in three representative lots of the commercial product. The table in Attachment 5 of the FCN is included as Appendix 1 to this memorandum. The averaged residue levels for some of the impurities (exception being those that were analyzed from paper extracts as described below) are summarized below in Table 2 (column 2). The analytical reports, including the test methods, are provided in Attachments 6-11 as described below.

We note that (b)(4) was identified as an impurity. (b)(4) is produced from the decomposition of the initiator (b)(4) during the polymerization procedure. (b)(4) is regulated for use as a polymerization catalyst in 21 CFR 176.170 (Components of paper and paperboard in contact with aqueous and fatty foods), and therefore, no exposure calculation for (b)(4) is necessary.

Attachment 6: Determination of (b)(4)), DEAM, (b)(4) (b)(4) , and telomer B alcohols by GC-FID[6]

[6] We note that the analysis was carried out on the commercial product that is the subject of this FCN as well as other products marketed by the notifier. Furthermore, the notifier did not explicitly provide the amount of sample used in the analysis. Nonetheless, the analytical report is adequate.

This method was based on extraction of the sample with acetonitrile (ACN) followed by filtration and GC analysis on a deactivated fused silica capillary column coated with Rtx-5 Amine (5% diphenyl/95% dimethylpolysiloxane). The separated components were detected by FID.

DEAM momomer and three decomposition products, (b)(4) and telomer B alcohol (from 62-FMA) were quantified on a weight percent basis using an external standard calibration. Telomer B alcohols included (b)(4)

Calibration Standards

(b)(4) calibration standards (0.05, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of (b)(4) (0.031 g (b)(4) diluted with ACN in a 25 mL volumetric flask) with ACN.

DEAM and (b)(4) calibration standards (0.005, 0.5, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.031 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

(b)(4) l calibration standards (0.08, 0.40, and 0.80 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.05 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

(b)(4) calibration standards (0.05, 0.25, and 0.50 mg/mL) were prepared by diluting a stock solution of the appropriate impurity (0.05 g impurity diluted with ACN in a 25 mL volumetric flask) with ACN.

Sampling and analysis

(b)(4) was weighed and placed in a vial. ACN (10 mL) was added and the contents sonicated. The ACN extract was filtered, transferred to a GC vial and sealed. An aliquot of the sample solution was injected into the GC and analyzed. The method was adequately validated. Two sets of data (from one plant batch and two pilot batches, and validation studies) were provided in Attachment 6.

Attachment 7: Determination of AA and MAA by GC-FID

This method was based on extraction of the sample with ACN followed by filtration and analysis by GC on an HP-5 capillary column fused silica coated with 5% phenylmethylsiloxane. The separated components were detected by FID.

Calibration Standards

AA and MAA calibration standards (100, 500 and 1000 ppm) were prepared by diluting a 10,000 ppm stock solution of the appropriate impurity with ACN.

Sampling and analysis

(b)(4) (2 g) was weighed and placed in a vial. ACN (10 mL) was added to the vial which was then sonicated. An aliquot was then transferred into a GC vial and analyzed. The method was adequately validated.

Attachment 8: Determination of residual telomer intermediates by GC/MS

This method determined the concentration of residual telomer intermediates in the FCS including:

- homologues of Telomer A: C6-I (perfluorohexyliodide), C8-I (perfluorooctyliodide), and C10-I (perfluorodecyliodide).

- homologues of Telomer B: C6 (6-2I; 1H,1H,2H,2H-perfluorooctyl iodide), C8 (8-2I; 1H,1H,2H,2H-perfluorodecyl iodide), and C10 (10-2I; 1H,1H,2H,2H-perfluorododecyl iodide).

- homologues of Telomer BA: C6 (6-2A; 1H,1H,2H,2H-perfluorooctan-1-ol), C8 (8-2A; 1H,1H,2H,2H-perfluorodecan-1-ol), C10 (10-2A; 1H,1H,2H,2H-perfluorododecan-1-ol).

- C8 Olefin (1H,1H,2H-perfluoro-1-decene).

- 8-2-8 Ester (2-(perfluorooctyl)ethylperfluorooctanoate).

Calibration Standards
Calibration standards of the telomer intermediates (0.1, 0.5, 1, 5, 10, and 20 ppm) were prepared by diluting a 20 ppm stock solution of the appropriate impurity with ACN.

Sampling and analysis
(b)(4) (200 mg) was weighed and placed in a vial. ACN (5 mL) was added, the contents sonicated, then transferred to a vial and analyzed by GC/MS. The method was adequately validated.

Attachment 9: Determination of residual perfluorocarboxylic acids (PFCAs) by LC/MS/MS

This method determined the concentration of residual PFCAs (C5 – C9) in (b)(4) PFCAs are present as anions, which are very soluble in water and methanol. The PFCAs were identified as perfluoropentanoic acid (C5 acid or PFPA), perfluorohexanoic acid (C6 acid or PFHxA), perfluoroheptanoic acid (C7 acid or PFHpA), perfluorooctanoic acid (C8 acid or PFOA), and perfluorononanoic acid (C9 acid or PFNA). The acids are quantified using LC/tandem mass spectrometry (LC/MS/MS) combined with a stable isotope isomer of PFOA (M+2) used as an internal standard analyzed in multiple reaction monitoring (MRM) mode.

Based on the manufacturing process of the FCS, which involved C6 chemistry, we would not expect significant levels of the other PCFAs to be present in the FCS.

Calibration Standards

Calibration standards of residual PFCAs (0.5, 1, 10, 25, 50 and 100 ppb) were prepared by diluting a stock solution of the appropriate PFCA with methanol.

Sampling and analysis
Samples (60 mg) were weighed and placed into 20 mL scintillation vials. Water was added and the samples were filtered, as needed. Sample (250 uL), water (250 uL), and internal standard (500 uL of a 50 ppb internal standard) were placed in an LC vial, and analyzed. The method was adequately validated.

Attachment 10: Determination of (b)(4) by GC-FID

This method was based on extraction of the sample with ACN followed by filtration and analysis by GC on a DB-1701 capillary column, crosslinked and surface bonded with 14% cyanopropylphenyl/ 85% dimethylpolysiloxane. The separated components were detected by FID.

Calibration Standards
Calibration standards of (b)(4) (50, 100, 500 and 1000 mg/L) were prepared by diluting a 10,000 mg/L stock solution of the appropriate impurity with ACN.

Sampling and analysis
(b)(4) (2 g) was weighed and placed in a vial. N,N-Dimethylacetamide, DMAC (10 mL) was added to the vial which was then sonicated. An aliquot was then transferred into a GC vial and analyzed. The method was adequately validated.

Attachment 11: Determination of (b)(4) by GC-FID[6]

This method was based on analysis of a sample (identified as (b)(4)) in tetrahydrofuran (THF) by GC on a fused-silica capillary column coated with a free fatty acid phase. The separated components were detected by FID.

Calibration Standards
A calibration standard of MEHQ (200 ppm) was prepared by diluting a stock solution of MEHQ with THF.

Sampling and analysis
(b)(4) was weighed and placed in a vial. THF (10 mL) was added to a vial which was then shaken. An aliquot was then transferred into a GC vial and analyzed by GC-FID. The method was adequately validated.

As noted above, impurities and residual levels in three batches of the commercial product are summarized in Appendix 1 to this memorandum. The average values for some of these impurities, as taken from Attachments 5 and 18, are shown in Table 2, below.

Table 2: Summary of Impurity Levels in the Commercial Product (19.5% solids)

Substance	Avg. Residual levels in commercial product
Monomers and LMWOs	
62-FMA	89 ppm (0.1% max)[a,b]
DEAM	100 ppm (0.03% max)[a]
MAA	<50 ppm
AA	<50 ppm
LMWOs	[c]
By-products	
(b)(4)	0.11 % (0.8% max)[a]
	418 ppm (0.08% max)[a,b]
	106 ppm
	0.015% (0.06 max)[a]
PFCAs and related substances	
(b)(4)	<0.5 ppm
	<0.5 ppm
	<0.5 ppm
	<0.5 ppm
	<0.6 ppm[d]
	<2 ppm
	<2 ppm
	<2 ppm
	<3.3 ppm[d]
	<2 ppm
	<2 ppm
	462 ppm (0.2% max)[a,b]
	<5 ppm
	<3.3 ppm
	<2 ppm
	<2 ppm
	58 ppm
	0.13%

[a] Maximum residual levels were taken from FDA Form 3480, Section II.B.3.
[b] Exposure to these impurities will be based on results of the exhaustive extraction described in the Migrant Levels in Food section below, rather than the residual levels reported in this table.
[c] Based on a LMWO fraction <2000 D of 0.045 wt.-%.
[d] C9 acid was detected in a single sample at 0.7 ppm, resulting in the average concentration of <0.6 ppm. Similarly, C6-2I was detected in two samples at 3-5 ppm, resulting in the reported average of <3.3 ppm. All other fluorinated acids and iodides were non-detected or below the limit of quantitation in all samples analyzed.

We have no questions on the manufacture of and impurities in the FCS.

Intended Use and Technical Effect

Information on the intended use and technical effect of the FCS is contained in Section II.D. of Form 3480, and Attachments 14-15.

The FCS is intended to be used as an oil and grease resistant treatment for paper and paperboard employed either prior to the sheet forming operation (aka wet-end) or at the size press. The FCS may be used at a level not to exceed 0.42 wt.-% of dry paper and paperboard intended for use in contact with all food types under Conditions of Use B through H and J (microwave susceptor applications). The proposed use is substitutional for the uses notified in DuPont's FCNs 206, 311, 338, and 646. As indicated in Attachment 18, the subject FCS is intended to replace the FCSs that are the subject of FCNs 206, 311, and 338.

In Section II.D.3, the notifier indicated that the utility of the FCS as an oil and grease resistant treatment was measured using established paper industry performance test procedures. The grease resistance test (TAPPI test method T 559 pm-96) was performed on treated and untreated paper sheets to demonstrate performance efficacy of the commercial product. This procedure was also used in FCN 311.

(b)(4)

base paper sheet exhibited a rating of less than 1. The notifier noted that these results clearly demonstrate the technical effect of the FCS as a grease resistance agent.

A technical information sheet for the commercial product is provided in Attachment 15. The suggested language for the FCN is contained in Attachment 14. We concur with this language.

We have no questions on the intended use and technical effect of the FCS.

Stability

In Form 3480, Section II.E., the notifier stated that, as indicated in the manufacturing process description in Attachment 4, a very small amount of hydrolysis of the polymer side chains may occur during post-polymerization, resulting in the formation of minor amounts of (b)(4) respectively.

The notifier noted that the thermal stability of the FCS was evaluated by thermogravimetric analysis (TGA) of the FCS from 0 to 235°C. The thermal stability of the FCS was also evaluated by NMR spectroscopic comparison of the dried polymer before and after exposure to high temperatures to simulate the proposed conditions of use (see Attachment 16). The TGA showed a weight loss of 3.98 wt.-%. Analysis by ^{13}C NMR before and after heating to 235°C did not indicate any change in the polymer structure.

We have no questions regarding the stability of the FCS under its intended conditions of use.

Migrant Levels in Food

The notifier did not carry out migration studies to support the proposed use. Rather, in Form 3480, Section II.F, the notifier calculated the worse-case migration of FCS oligomers and impurities based on measured levels in the commercial product or from extraction studies conducted on paper manufactured from the FCS are described below.

Attachment 17 contains the results of exhaustive extractions of paper manufactured with the FCS using chloroform ($CHCl_3$) as the extraction solvent. The extracts were analyzed for (b)(4) (b)(4) calibration standards (50, 100 and 1000 ng/mL) were prepared by diluting a 1000 µg/mL stock solution of the appropriate impurity with $CHCl_3$.

Paper samples (two 8.5"x11" sheets, 59 g/m^2) treated at the size press with the FCS (0.42% by weight) were Soxhlet extracted with $CHCl_3$ (56.7 mL) for 6 hours and the resulting extracts analyzed by GC/MS for impurities. The same paper samples were extracted a second time for 4 hours with fresh $CHCl_3$ (56.7 mL). The average level of 62-FMA was 84 ng/mL (or 0.0255 $\mu g/in^2$ paper sample), 6-2 alcohol was 38 ng/mL (or 0.0115 $\mu g/in^2$ paper sample), and 6-2/6-2 ether was 40 ng/mL (or 0.0121 $\mu g/in^2$ paper sample). The method was adequately validated. Results are presented in Table 2, above.

Consumer Exposure

Information on consumer exposure is contained in Form 3480, Section II.G, and Attachments 18-20. The notifier used the results of the GPC analysis of TNEs, the residue levels determined by direct analysis of the commercial product (Table 2, column 2), and extraction of paper manufactured from the FCS, to determine migration to food. Exposure estimates are provided in

Table 3, below.

Low molecular weight oligomers (LMWOs)

In Attachment 18, the notifier calculated the worst-case migration, <M>, of LMWOs based on a MW <2000 D (0.045 wt.-%), and the maximum FCS use level (0.42% on the polymer solids basis). For Conditions of Use B through H, the notifier assumed a typical food-contact paper basis weight of 0.05 g/in^2 (50 mg/in^2) and our default food mass-to-surface area ratio of 10 g food/in^2. For use condition J, the notifier assumed a paper basis weight of 0.023 g/in^2 (a typical paper weight for microwave susceptors applications), and a food ratio of 5 g/in^2 as follows:

$<M>_{Oligomers, B-H}$ =
= (0.00045 g oligmers/g FCS)(0.0042 g FCS/g paper)(0.05 g paper/in^2)(1 in^2/10 g food)
= 9.5×10^{-9} g oligomers/g food or 9.5 ppb

$<M>_{Oligomers, J}$ =
= (0.00045 g oligmers/g FCS)(0.0042 g FCS/g paper)(0.023 g paper/in^2)(1 in^2/5 g food)
= 8.7×10^{-9} g oligomers/g food or 8.7 ppb

The notifier then indicated that migration data previously submitted for the closely related polymer that was the subject of FCNs (b)(4) (a copolymer of a 2-perfluoroalkylethyl acrylate with a range of $(CF_2)_n$ groups where n= 3-19, DEAM and glycidyl methacrylate, marketed as Zonyl 9464/9594 HP product) demonstrated that only a portion of the oligomers present migrate to 10% ethanol when tested under Condition of Use B. Specifically, the migration studies described in FCN 206 were conducted on paper samples (basis weight 0.036 g/in^2) containing 0.33% of polymer. The oligomer content of the FCS in FCN (b)(4) was 0.84%, and testing resulted in 25 ppb migration of oligomers to 10% ethanol.

Assuming that 100% of the available oligomers migrated to food, the worst-case migration for the samples tested would be 100 ppb or (0.0084 g oligomers/g FCS)x(0.0033 g FCS/g paper)x(0.036 g paper/in^2)x(1 in^2/10 g food). Thus, the actual measured migration of 25 ppb represents a ¼ (or 25%) of the migration of the oligomer content of the polymer in FCN 206. The notifier applied this rationale to the present FCN to determine a migration of oligomers (from the subject FCN) to aqueous food, under Conditions of Use B, of 2.4 ppb as follows.

$<M>_{Oligomers, B-H, aqueous foods}$ = 9.5 ppb x 25% = 2.4 ppb

In Attachment 20, the notifier used the <M> values calculated above, the applicable CFs (0.05 for specialty paper and 0.001 for microwave susceptor applications), and food-type distribution factors (for Conditions of Use B through H) to estimate a dietary concentration (DC) as follows:

$DC_{B-H} = CF_{specialty\ paper} \times <M>_{B-H}$ = 0.05 x [(2.4 ppb x 0.59) + (9.5 ppb x 0.41)]
= 0.05 x 5.3 ppb = 0.27 ppb

$DC_J = CF_{microwave\ susceptor} \times <M>_J$ = 0.001 x 8.7 ppb = 0.009 ppb

$DC_{Total} = DC_{B-H} + DC_J = 0.27$ ppb + 0.009 ppb = 0.28 ppb

(b)(4)

For the impurities determined in the exhaustive extraction described in Section II.F, the notifier calculated migration levels to food based on the extracted levels from the treated paper samples (basis weight of 59 g/m^2 or 0.038 g/in^2). The notifier first applied a correction factor to the measured levels of the three analytes to account for differences in the paper basis weight (0.05 g/in^2 for condition B through H and 0.023 g/in^2 for condition J) as follows:

<M>(b)(4): (b)(4) = 3.4 ppb

<M>(b)(4): (b)(4) = 3.1 ppb

The <M> for (b)(4) is 1.5 and 1.4 ppb for conditions B through H, and J, respectively, and <M> for (b)(4) is 1.6 and 1.5 ppb for conditions B through H, and J, respectively.

The notifier then used the <M> values and the applicable CFs to estimate exposure.

(b)(4)

In Attachment 18, the notifier indicated that (b)(4) was used as a monomer in the closely related polymer that was the subject of DuPont's (b)(4) (b)(4) and that the maximum residual specification for (b)(4) in the finished product in the subject FCN is identical to that in the previous notifications. The notifier indicated that in FCN (b)(4) the DC for (b)(4) was 0.14 ppb. This exposure was based on the results of migration testing conducted under condition of use B. The FCS in FCN (b)(4) is used at levels up to 0.69%, whereas the subject FCS is limited to a maximum of 0.42%. Therefore, the previously calculated exposure can be adjusted by a factor of 0.61 (or 0.42/0.69) to calculate a DC for (b)(4) from the subject FCN. The DC for (b)(4), under Conditions B through H, would be 0.085 ppb (or 0.61 x 0.14 ppb).

For use in microwave susceptor applications, the notifier calculated a DC assuming 100% migration, as described below.

Other impurities

For the remaining impurities that may be present in the commercial product, the notifier estimated exposure based on the average concentrations measured in the commercial product containing 19.5% polymer solids (shown in Table 2 above). The notifier first converted the concentrations in the commercial product to concentrations in the polymer solid (by dividing by a factor of 0.195). The notifier then used the maximum FCS use level (0.42% on the polymer solids basis) and the applicable paper basis weight, food mass-to-surface area ratio and CF to estimate exposure. Exposure estimates are provided in Table 3, below. We concur with the notifier's approach and

with the notifier's exposure estimates.

Table 3: Exposure estimates

Substance	$<M>_{B-H}$ (ppb)	$<M>_{J}$ (ppb)	DC_{B-H} (ppb)	DC_{J} (ppb)	DC_{Total} (ppb)
Monomers and LMWOs					
62-FMA	3.4[a]	3.1[a]	0.17	0.0031	0.17
DEAM		9.9	0.085[b]	0.0099	0.095
MAA	<5.4	<5	<0.27	<0.005	<0.27
AA	<5.4	<5	<0.27	<0.005	<0.27
LMWOs	5.3[c]	8.7[c]	0.27	0.009	0.28
By-products					
(b)(4)	120	110	5.9	0.11	6
	1.6[a]	1.5[a]	0.08	0.0015	0.08
	11.4	10.5	0.57	0.01	0.58
	[d]	[d]			
PFCAs and related substances					
(b)(4)	<0.054	<0.05	<0.0027	<0.00005	<0.0028
	<0.054	<0.05	<0.0027	<0.00005	<0.0028
	<0.054	<0.05	<0.0027	<0.00005	<0.0028
	<0.054	<0.05	<0.0027	<0.00005	<0.0028
	<0.065	<0.059	<0.0032	<0.00006	<0.0033
	<0.215	<0.20	<0.011	<0.0002	<0.011
	<0.215	<0.20	<0.011	<0.0002	<0.011
	<0.215	<0.20	<0.011	<0.0002	<0.011
	<0.36	<0.33	<0.018	<0.00033	<0.018
	<0.215	<0.20	<0.011	<0.0002	<0.011
	<0.215	<0.20	<0.011	<0.0002	<0.011
	1.5[a]	1.4[a]	0.075	0.0014	0.076
	<0.54	<0.50	<0.027	<0.0005	<0.028
	<0.36	<0.33	<0.018	<0.00033	<0.018

(b)(4)					
	<0.215	<0.20	<0.011	<0.0002	<0.011
	<0.215	<0.20	<0.011	<0.0002	<0.011
(b)(4)					
	Essentially zero				
	Essentially zero				

[a] Based on the results of the exhaustive extraction described in the Migrant Levels in Food section.
[b] Based on the discussion presented in the Exposure section.
[c] Based on a LMWO fraction <2000 D of 0.045 wt.-%.
[d] As indicated in the impurity section above, (b)(4) is produced from the decomposition of the (b)(4) during the polymerization procedure. Since (b)(4) is regulated for use as a polymerization catalyst in §CFR 176.170, no exposure calculation for (b)(4) is necessary.

We have no questions on consumer exposure.

Notification Language

The acknowledgment letter, signed off by Chemistry on May 6, 2009, is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb: FCN885_C_memo
RDInit: ABBailey, 5-12-09
Final: seb, 5-14-09

Appendix

Appendix 1- Summary of Residue Results From Attachment 5 of FCN 885

Analyte	Synonym	Attachment No.	Plant Batch 2	Pilot Batch 4	Pilot Batch 5
(b)(4)		9	<0.5 ppm	<0.5 ppm	<0.5 ppm
		9	<0.5 ppm	<0.5 ppm	<0.5 ppm
		9	<0.5 ppm	<0.5 ppm	<0.5 ppm
		9	<0.5 ppm	<0.5 ppm	<0.5 ppm
		9	<0.5 ppm	0.7 ppm	<0.5 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	<2 ppm	3 ppm	5 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	397 ppm	437 ppm	551 ppm
		8	11 ppm	<2 ppm	<2 ppm
		8	6 ppm	<2 ppm	<2 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		8	<2 ppm	<2 ppm	<2 ppm
		6	55 ppm	107 ppm	105 ppm
		6	389 ppm	446 ppm	418 ppm
		6	100 ppm	105 ppm	94 ppm
		6	0.126%	0.106%	948 ppm
		7	<0.005 %	<0.005 %	<0.005 %
		7	<0.005 %	<0.005 %	<0.005 %
		11	88.8 ppm	137 ppm	92.7 ppm
		6	0.017%	0.013%	0.013%
		10	29 ppm	50 ppm	95 ppm
		10	0.115%	0.087%	0.179%

CHEMOURS FCN 940

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Hexane, 1,6-diisocyanato-, homopolymer, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octanol-blocked

2. CAS Registry Number

357624-15-8

3. Trade or Common Name

(b) (4) [redacted] CONFIDENTIAL

4. Other Chemical Names *(IUPAC, etc*

Hexamethylene diisocyanate homopolymer, 2-Perfluorohexylethyl alcohol blocked

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a reaction product of hexamethylene diisocyanate (HMDI) homopolymer with 2-perfluorohexylethyl alcohol. The structural formula and molecular formula for the polymer are shown in **Attachment 1**.

The starting monomers used in the manufacture of the FCS are identified in the following table. See **Attachment 1** for typical ratios of monomer units:

CASRN	CAS Name	Common Name
28182-81-2	Hexane, 1,6-diisocyanato-, homopolymer	HMDI
647-42-7	1-Octanol, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-	6-2 Alcohol

The commercial product consists of an aqueous dispersion of the polymer containing approximately (b) [redacted] solids. See **Attachment 1** for typical formulation details.

The FCS has a minimum number-average molecular weight (Mn) of (b) [redacted] For details of molecular weight analyses on the polymer, see the analytical report set forth in **Attachment 2**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Representative NMR (^{1}H, ^{13}C, and ^{19}F) spectra are provided in **Attachment 3**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
Hexane, 1,6-diisocyanato-, homopolymer	28182-81-2	Monomer	☐ Yes ☒ No
1-Octanol, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-	647-42-7	Monomer	☒ Yes ☐ No
(b) (4) [redacted]			☒ Yes ☐ No
			☒ Yes ☐ No
			☐ Yes ☒ No
			☒ Yes ☐ No
			☒ Yes ☐ No
			☒ Yes ☐ No
CONFIDENTIAL		CONFIDENTIAL	

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 4** for a description of the manufacturing process.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
2-Perfluorohexylethyl alcohol (6-2 alcohol)	647-42-7	**See Attachment 5**	0.1	☐ Yes ☐ No (*)
				☐ Yes ☐ No
(b) (4) [redacted]		**See Attachment 5**	--	
		See Attachment 5	--	☐ Yes ☐ No
		See Attachment 5	0.1	☐ Yes ☐ No
		See Attachment 5	--	
		<0.5 ppm	0.0002	☐ Yes ☐ No
		<18 ppm	--	☐ Yes ☐ No
		181 ppm	--	☐ Yes ☐ No

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(*) The boxes in the right-hand column above are not checked because it is not certain whether migration of impurities will occur. Nonetheless, the maximum levels at which the compounds could migrate to food are calculated as noted in section II.F.2 below.

The impurity concentrations are expressed in terms of the concentration in the commercial product, i.e., the aqueous dispersion containing (b) [redacted] solids. See **Attachment 5** for summary data on typical impurity levels.

Note (1): (b) (4) [redacted]

(b) (4) [redacted]

See **Attachments 6, 7, 8, 9, and 10** for analytical reports including the test methods used by the Notifier to determine residual starting reactants and various impurities in the finished product and the results of representative batch analyses, including raw data. As only a single pilot plant batch has been produced to date, data are included from analysis of this pilot batch and two laboratory-scale production batches. The pilot batch is identified in the analytical reports as (b) (4) [redacted] while the laboratory batches are referred to as (b) (4) [redacted]

Note that the summary data in **Attachment 5** includes analytical results for several additional (b) (4) [redacted]

(b) (4) [redacted]

Residual concentrations of the (b) (4) [redacted] Each of these compounds has an explicit FDA clearance that encompasses the intended use in the manufacture of the FCS. Thus, they are not considered further here.

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† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
N/A	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Number-average molecular weight (Mn) (Daltons)	--	(b) (4)	(b) (4)
Fraction <2000 Daltons (wt-% of polymer solids)	20	--	
Solids Content (wt-%)			
Particle Size (nm)			
Density (g/mL)			
pH			
Flash Point (°F)			
Viscosity (cP @ 23°C)			
Appearance			

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Additional specifications regarding maximum impurity levels are set forth in Section II.B.3 above; analytical methods for measuring these impurity levels are provided in **Attachments 6–8.** The methods used to determine number-average molecular weight and the weight-fraction below 2000 Daltons are set forth in **Attachment 2**. Test methods used to determine additional physical property specifications are set forth in **Attachment 13** of FCN (b) .

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

GPC analyses have been conducted on samples of the FCS to determine the level of low molecular weight oligomers (LMWO) below 2000 Daltons. (Due to the fluorinated nature of the polymer, we have used 2000 Daltons rather than 1000 Daltons as the upper cut-off for determining the oligomer content to account for the comparatively high mass of the polymer relative to molecular size.) The LMWO content below 2000 Daltons was conservatively estimated based on the assumption that a late-eluting peak that overlapped with the main polymer peak consisted entirely of oligomers below 2000 Daltons. See **Attachment 2** for details of the analyses.

The available pilot lot of the FCS was analyzed as the liquid emulsion product, and found to contain 17.3% of LMWO by weight of polymer solids. (b) (4)

(b) (4)

In addition to these analyses, two laboratory-produced lots of the FCS were also subjected to GPC analysis. These samples were found to contain (b) (4)

Based on the entirety of the GPC data, a conservative estimate of the LMWO content is 17.3%, the level found in the pilot lot sample analyzed as the emulsion with no further sample preparation.

Based on the available data, we will use an estimated LMWO content of **17.3%** to calculate worst-case migration of FCS oligomers to food.

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☐ Repeat Use

The FCS copolymer is intended for use as an oil and grease resistant treatment for paper and paperboard intended for use in contact with food. The treatment may be applied either in the wet-end or at the size press. The copolymer is intended for use at levels not to exceed 0.18 wt.% of polymer solids by weight of the paper. The food-contact substance is intended to contact all types of food under Conditions of Use B through H. The food-contact substance is intended for single-service use.

Suggested language for listing this FCN on FDA's "Inventory of Effective Food Contact Substance Notifications" is set forth in **Attachment 11**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE
The FCS will be used to treat paper at levels not to exceed 0.18 wt.% of polymer solids by weight of the paper.	All types of food (Types I through IX)	Conditions of Use B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

(b) (4) CONFIDENTIAL is intended to impart oil and grease resistance to paper and paperboard used in food-contact applications. The utility of the product as an oil and grease resistant treatment was measured using established paper industry performance test procedures. The grease resistance test (TAPPI test method T 559 pm-96) was performed on base and treated paper sheets to demonstrate performance efficacy of (b) (4) (a description of this test is provided in FCN No. 206, Appendix VI). The application procedure and results are described below.

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Thirty-two-pound base paper sheet was treated with sizing solution containing 4% ethylated starch ((b) (4) and 0.7 wt% of (b) (4) at 158°F, using a laboratory size press. (Note: the application rate is expressed in terms of the commercial product, which contains approximately (b) of polymer solids. Thus, the paper was treated at a level corresponding to 0.2% by weight of polymer solids on the paper.) The treated paper sheet was subsequently dried by a laboratory drum drier at 235°F. The dried paper contained (b) (4). The treated paper sheet gave a repellency rating of 5, indicative of moderate grease repellency. The untreated base paper sheet gave a rating of less than 1. These results clearly demonstrate the technical effect delivered by (b) (4) M as a grease resistance agent.

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For additional information on technical utility, see the Technical Information Sheet and Material Safety Data Sheet set forth in **Attachment 12**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

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The FCS is stable under the conditions of intended use. To evaluate the thermal stability of (b) (4), polymer solids were analyzed by thermogravimetric analysis. To water (1600 g), sodium chloride (400 g), and methanol (600 g) stirred in a 4 L beaker at room temperature, (b) (4) (500 g) was added over 1 hour. The solution was stirred for 3 hours and precipitate was filtered using a Buchner funnel. The solid was washed with 3 L of warm water (40°C) followed by 1 L of D.I. water and dried in a vacuum oven (2 torr) at 40°C until constant mass was obtained (4 days), yielding 141 g of polymer (98%). The material was analyzed by TGA from room temperature to 600°C at 10°C/min.

A report of this testing appears in **Attachment 13**. As shown there, the polymer was stable at temperatures up to 200°C, above which measurable weight loss was found; approximately 64% weight loss of the polymer was measured at 350°C. The data confirm the heat stability of the polymer under the conditions of its intended use.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II – CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
STRUCTURE		**STRUCTURE**	
SUBSTANCE NAME	**CAS REG. NO.**	**SUBSTANCE NAME**	**CAS REG. NO.**
STRUCTURE		**STRUCTURE**	

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration testing has not been carried out. Instead, worst-case migration of FCS oligomers and potential impurities has been calculated based on measured levels in the product. See Section II.F.2 below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
N/A					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

No migration testing has been conducted, as stated previously. However, the analytical studies conducted to determine residual starting reactants and other impurities in the FCS have been validated. See **Attachments 6-9** for data validating the analytical methods.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

Due to space limitations, the worst-case migration calculations are set forth in **Attachment 14.**

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The worst-case migration levels calculated in **Attachment 14** may be multiplied by the applicable consumption factor (CF) to calculate the corresponding concentrations at which FCS components may enter the diet. See **Attachment 15** for these calculations. The resulting worst-case dietary exposure levels are shown in Section II.G.3 below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
FCS Oligomers	--	See Attachment 14	78 ppb	0.23 mg/day	78 ppb
			CONFIDENTIAL		
(b) (4) [redacted]		See Attachment 14	$< 7.5 \times 10^{-4}$	$< 2.3 \times 10^{-6}$	
		See Attachment 14	$< 3.75 \times 10^{-3}$	$< 1.1 \times 10^{-5}$	
		See Attachment 14	0.03	9.0×10^{-5}	
		See Attachment 14	$< 3.75 \times 10^{-3}$	$< 1.1 \times 10^{-5}$	
		See Attachment 14	0.94	0.0028	
		See Attachment 14	0.045	1.4×10^{-4}	
		See Attachment 14	0.097	2.9×10^{-4}	

CONFIDENTIAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: February 16, 2010

From: Division of Food Contact Notifications
Chemistry Team II

Subject: FCN 940: Hexane, 1,6-diisocyanato-, homopolymer, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-l-octanol-blocked as a grease-proofing agent on paper and paperboard.

To: Division of Food Contact Notifications
Regulatory Team II
Attn: P. Honigfort, Ph.D.

DuPont Chemical Solutions Enterprise, through Keller and Heckman, L.L.C., submitted this food contact notification (FCN) dated 9/30/2009 and update dated 12/4/2009 for the use of hexane, 1,6-diisocyanato-, homopolymer, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-l-octanol-blocked as a grease-proofing agent on paper and paperboard.

Background and Regulatory Status of the FCS

The food contact substance (FCS) is not currently regulated or authorized for use in contact with food. There are a number of perfluoro-polymer-based grease-proofing agents regulated or authorized for use in contact with food.

Identity

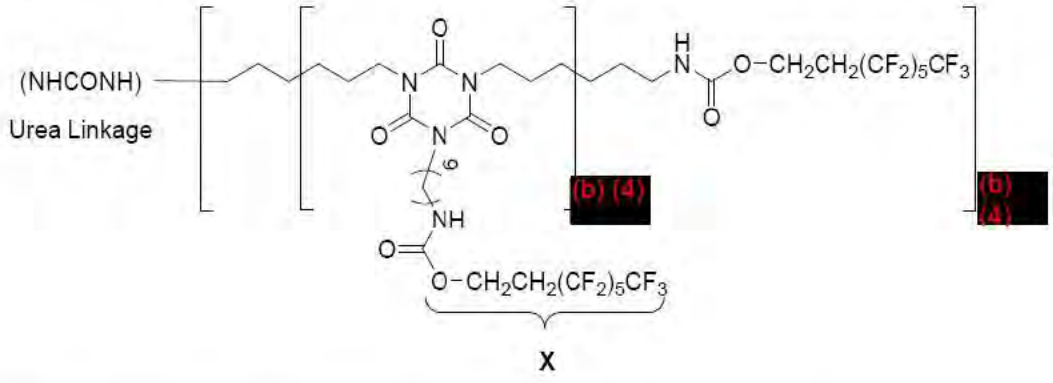
CAS Name: Hexane, 1,6-diisocyanato-, homopolymer, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-l-octanol-blocked

CAS Reg. No.: 357624-15-8
Trade Names: (b) (4)
Other Names: Hexamethylene diisocyanate homopolymer, 2-Perfluorohexylethyl alcohol blocked

Molecular weight: minimum <Mn> greater than (b) (4)

The notifier did not provide the weight-average molecular weight for their material. The percentage of oligomers below 2000 Daltons is reported as 17%.

Structure:



The corresponding molecular formula is $(C_{16}H_{24}N_4O_4)_m$ $(C_8H_5F_{13}O)_n$.

The typical ratios of the starting monomers used in the manufacture of the FCS are set forth in the following table.

CASRN	CAS Name	Typical Mole %	Typical Weight %
28182-81-2	Hexane, 1,6-diisocyanato-, homopolymer	(b) (4)	
647-42-7	1-Octanol, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-		

The notifier provided NMR (^1H, ^{13}C, and ^{19}F) spectra in Attachment 3 of the FCN. From the data provided, it appears that the fluorine NMR is (b) (4) (b) (4) (b) (4). The supporting spectra are consistent with the chemical structure of the FCS.

Manufacture

(b) (4)

(b) (4)

(b) (4)

[redacted]

[redacted]

Component	Relative Concentration (Wt%)
6-2 Alcohol	(b) (4)
HMDI Prepolymer	
(b) (4)	

(b) (4)

[redacted]

(b) (4)

[redacted]

We have no questions regarding the manufacture of the FCS.

Stability

The notifier isolated the FCS from the aqueous dispersion and performed a thermogravimetric analysis on the isolate. The FCS is stable up to 200 °C and demonstrates a loss of 5 weight-percent at 275 °C. The FCS is stable under the intended conditions of use.

(b) (4)

[redacted]

Intended Use/Use Level and Intended Technical Effect
The FCS copolymer is intended for use as an oil- and grease-resistant treatment for paper and paperboard intended for use in contact with food. The treatment may be applied either in the wet end or at the size press. The copolymer is intended for use at a level not to exceed 0.18 weight-percent of polymer solids by weight of the paper. The food-contact substance is intended to contact all types of food under Conditions of Use B through H. The food-contact substance is intended for single-service use.

Migration Studies
The notifier did not conduct migration studies in support of this notification. Instead, they analyzed the finished food contact substance for oligomers and impurities and used these values, along with the use level, and an assumption of 100% migration to estimate exposure to the FCS and its impurities.

Oligomers
The notifier analyzed three samples of the FCS using gel permeation chromatography equipped with a low-angle laser light scattering detector and a refractive index detector. The notifier then used a curve-fitting program (Origins) to estimate the quantity of oligomers below 2000 Daltons. Figure 4 in Attachment 2 to the notification shows four overlapping curves. The black curve is the original chromatogram of the FCS, the green curves are the two Gaussian curves that were fit to the black curve using the curve-fitting program. The red curve is the summation of the two green curves between 62 and 65 minutes, the expected retention time of the oligomers below 2000 Daltons. The percentage of oligomers was calculated by dividing the area under the red curve by the sum of the areas under the two green curves. The notifier verified in their 12/4/2009 update to the notification that our interpretation of these data was correct and provided additional information on their calculations. We have reviewed the data and agree with the notifier's conclusions that 17% of the FCS has molecular weight of less than 2000 Daltons. As this is a highly fluorinated polymer, we calculated the molecular weight adjusted 1000 Dalton cutoff value for oligomers. In this case, the value is 1600 Daltons. As we do not have access to the curve-fitting program and the value that the notifier calculates is more conservative, we will rely on the notifier's estimation of the quantity of oligomers below 2000 Daltons for our exposure estimates.

(b) (4) (Attachment 6)
The notifier analyzed, in triplicate, the finished FCS for residual quantities of (b) (4) using liquid chromatograph/tandem mass spectrometry combined with a stable isotope isomer of (b) (4) as an internal standard. The notifier prepared 6 standard solutions of each (b) (4) ranging in concentration from 0.5 to 100 ppb (correlation coefficients for each of the calibration curves were greater than 0.996). Each standard contained 25 ppb of the isotopically labeled (b) (4) The method was validated by spiking samples of the FCS with 2.5, 5, and 10 ppb of the (b) (4) The percent recoveries for each of the (b) (4) are acceptable. Although the notifier did not spike at the limit of detection (LOD), we consider the LOD valid as it is the lowest point on the calibration curve. The (b) (4) were not detected above the limit of detection (LOD = 0.5 μg/g dispersion, or <1.7 μg/g dry polymer) in any of the samples.

(b) (4) (Attachment 7)[4]

The notifier analyzed, in triplicate, the finished FCS for residual quantities of (b) (4) using gas chromatography/mass spectrometry. The notifier prepared 4 standard solutions of each analyte ranging in concentration from 0.1 to 20 µg/mL (correlation coefficients for each of the calibration curves were greater than 0.995). The method was validated by spiking samples of the FCS with 2.5, 5, and 10 µg/mL of each analyte. The percent recoveries for each of the analytes are acceptable. Although the notifier did not spike at the limit of detection (LOD), we consider the LOD valid as it is the lowest point on the calibration curve. None of the analytes was detected above the limit of detection (LOD = 2.5 µg/g dispersion or <8.3 µg/g dry polymer) in any of the samples except for (b) (4) which had an average concentration of 20 µg/g dispersion, or 67 µg/g dry polymer.[5]

(b) (4) (Attachment 8)[4]

The notifier analyzed, in triplicate, the finished FCS for residual quantities of (b) (4) (b) (4) ether using gas chromatography/mass spectrometry. The notifier prepared 4 standard solutions of each analyte ranging in concentration from 1-100 ppm (correlation coefficient, 0.996). The method was validated by spiking samples of the FCS with 500, 1000, 2500 ppm of (b) (4) The percent recoveries for each of the analytes are acceptable. (b) (4) was detected in all of the samples at an average concentration of 627 µg/g dispersion, or 2090 µg/g of dry polymer.

Attachment 9)[4]

The notifier analyzed, in triplicate, the finished FCS for residual quantities of (b) (4) (b) (4) using gas chromatography/mass spectrometry. The notifier prepared 5 standard solutions of each analytes ranging in concentration from 0.06-2.3 ppm (b) (4) (correlation coefficient, 1) and from 0.4-16.7 ppm (b) (4) (correlation coefficient, 0.994). The method was validated by spiking samples of the FCS with 0.58, 1.16, and 1.74 µg (b) (4) /mL and 4.19, 8.37, and 12.56 µg (b) (4) /mL of the analytical solution. The percent recoveries for the analytes are acceptable. (b) (4) were detected in all of the samples at an average concentration of 30 µg/g (101 µg/g dry polymer) and 64 µg/g (215 µg/g dry polymer) of commercial product, respectively.

The notifier synthesized the mono and (b) (4) in their laboratory. The material was characterized by ^{1}H and ^{13}C-NMR spectroscopy and the relative concentrations of each adduct determined from these analyses. Supporting data for these analyses were provided in the 12/4/2009 update to the notification.

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4 The notifier did not provide sufficient supporting data in Attachments 7, 8, 9 and 10 of the notification that would allow us to verify the calibration curves presented in these attachments. In addition, the notifier did not provide appropriate validation data for the method presented in Attachment 10 of the notification. The requested data were provided in the 12/4/2009 update to the notification.

5 Although the notifier did not spike at our recommended ½, 1 and 2 times the measured quantity of the analyte, we have no reason to doubt the validity of the measurements given the data presented in the notification.

(b) (4) (Attachment 10)[4]

The notifier analyzed, in triplicate, the finished FCS for residual quantities of (b) (4) (b) (4) and (b) (4) using gas chromatography/mass spectrometry. The notifier prepared 5 standard solutions of each analyte ranging in concentration from 10-258 ppm (b) (4) (correlation coefficient, 0.992) and from 10-246 ppm (b) (4) (correlation coefficient, 0.997). The method was validated by spiking samples of the FCS with 10, 26, and 52 ppm (b) (4) and 10, 26, and 49 ppm (b) (4) The percent recoveries for each of the analytes are acceptable. Although the notifier did not spike at the limit of detection (LOD) for (b) (4) we consider the LOD valid as it is the lowest point on the calibration curve. (b) (4) was not detected in the finished FCS above the LOD of 20 μg/g of the dispersion, the lowest point on the calibration curve. (b) (4) was detected at an average concentration of 139 μg/g of the dispersion.[6]

The worst-case migration of the FCS to food is calculated using: 1) our standard assumption for the basis weight of paper and paperboard (0.05 g.in^2, 2) the maximum use level of the FCS on paper and paperboard (0.0018 g FCS/g paper), 3) the concentration of oligomers below 2000 Daltons (17%), 4) the assumption that 100% of the oligomers below 2000 Daltons migrate into food, and 5) our standard assumption that 10 grams of food contacts 1 square inch of food packaging.

$$[(0.05\text{g paper/in}^2) \times (0.0018\text{ g FCS/g paper}) \times (0.173\text{ g oligomers/g FCS})]/10\text{ g food/in}^2 = 1.56 \times 10^{-6}\text{ g oligomers/g food, or } 1560\ \mu\text{g/kg food.}$$

The worst-case migration of the impurities of the FCS are estimated using assumptions 1,2,4, and 5 above and the weight percentage of solids in the FCS (30%). A sample calculation for (b) (4) is shown below.

$$[(0.05\text{g paper/in}^2) \times (0.0018\text{ g FCS/g paper}) \times (0.5 \times 10^{-6}\text{g (b) (4) g FCS}) \times (1/0.3)]/10\text{ food/in}^2 = 1.5 \times 10^{-11}\text{ g oligomers/g food, or } 0.015\ \mu\text{g/kg food.}$$

Exposure Estimates

The dietary concentrations (DC) of the low-molecular weight oligomers and the impurities in the FCS are calculated by multiplying the concentration in food by the consumption factor for new polymers (0.05). The estimated daily intakes (EDI) for each of the potential migrants is calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day. An example using for the oligomers is shown below. DCs and EDIs for the remaining migrants are calculated in the same fashion.

$$\text{DC} = (0.05)(1560\ \mu\text{g/kg food}) = 7.8\ \mu\text{g/kg food}$$
$$\text{EDI} = (3\text{ kg food/p/d})(7.8\ \mu\text{g/kg food}) = 230\ \mu\text{g oligomers/p/d}$$

6 Re-evaluation of the notifier's data revealed a small error in their calculations. We have re-evaluated the data and provided a corrected concentration for (b) (5)

Exposure Estimates

Compound	Migration (µg/kg)	DC (pptr)	EDI (ng/p/d)
Oligomers	1.56 mg/kg food	78 ppb	230 µg/p/d
(b) (4)	<0.015	0.75	2.3
	<0.015	0.75	2.3
	<0.015	0.75	2.3
	<0.015	0.75	2.3
	<0.015	0.75	2.3
(b) (4)	<0.075	3.75	11
	<0.075	3.75	11
	<0.075	3.75	11
	<0.075	3.75	11
(b) (4)	0.60	30	90
	<0.075	3.75	11
	<0.075	3.75	11
(b) (4)	<0.075	3.75	11
	<0.075	3.75	11
	<0.075	3.75	11
	18.8	0.94 ppb	2.8 µg/p/d
(b) (4)	0.9	0.045 ppb	0.14 µg/p/d
	1.9	0.1 ppb	0.3 µg/p/d
(b) (4)	0.6	30	90
	4.17	208.5	625

Cumulative Exposure

The exposures to the (b) (4) as well as the (b) (4) (b) (4) (b) (4) re equal to or less than what was calculated in FCN (b) (4). As the uses for this FCS are substitutional for those in FCN (b) (4) (condition of use B-H, and J); there will be no increase in their respective cumulative exposures. As for (b) (4) (b) (4) (DC = 30 pptr), a review of the FCNs covering grease-proofing agents reveals that exposure to (b) (4) was not typically calculated, but rather, exposure to total (b) (4) was provided. In FCN (b) (4), exposure to total (b) (4) was 0.69 µg/p/d, or 23 ppb. Given the 30 pptr exposure to (b) (4) from this use and the substitutional nature, the 23 ppb exposure to total from FCN (b) (4) will subsume the exposure to (b) (4) calculated for the FCN.

Kirk Arvidson, Ph.D.

HFS-275 (Chemistry Reading File)
HFS-275: KBArvidson:436-1152:FCN000940_C_MEMO: 2/3/2010
R/D Init: MAAdams: 2/16/2010
Final: kba:2/16/2010

(b4) (6)

Kirk Arvidson, Ph.D.

HFS-275 (Chemistry Reading File)
HFS-275: KBArvidson:436-1152:FCN000940_C_MEMO: 2/3/2010
R/D Init: MAAdams: 2/16/2010
Final: kba:2/16/2010

CHEMOURS FCN 1027

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2-propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate

2. CAS Registry Number

1071022-26-8

3. Trade or Common Name

(b)(4) **CONFIDENTIAL**

4. Other Chemical Names *(IUPAC, etc*

Acetate salts of methacrylic acid copolymer with acrylic acid, diethylaminoethyl methacrylate, and 2-(perfluorohexyl)ethyl methacrylate

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is fully described in FCN 885. For ready reference, the basic descriptive information set forth in Part II, Section A.5 of FCN 885 is reproduced below.

The starting monomers used in the manufacture of the FCS are as follows:

(b)(4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Representative IR and NMR (^{1}H and ^{13}C) spectra are provided in Attachment 3 of FCN 885.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†

Information on the substances used in the manufacture of the FCS is provided in FCN 885 and is incorporated by reference. Please see **Attachment 2** of this FCN for additional information.

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

The manufacturing process for the FCS was described in Attachment 4 of FCN 885. Some minor changes in the process are described in **Attachment 2** of this notification.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
See **Attachment 3**				

A full impurity profile for the FCS was provided in FCN 885. Additional analyses have been conducted on FCS lots that were produced by the slightly modified manufacturing process described in **Attachment 2** of this notification. Please see **Attachment 3** for a tabulation of the impurity concentrations measured in these samples. The analytical methods used to determine impurities in the FCS were fully described in FCN 885; please see Attachments 6-11 of FCN 885 for the analytical methodology and validation of the test methods. Raw data from the new analyses, including peak integrations and representative chromatograms or other instrument output, are set forth in a supplemental report presented in **Attachment 4**.

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
N/A	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES

(b)(4) [redacted]

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

GPC analyses presented in FCN 885 indicated a low molecular weight oligomer (LMWO) content below 2000 Daltons of (b)(4) by weight of polymer solids. (Due to the fluorinated nature of the polymer, we have used 2000 Daltons rather than 1000 Daltons as the upper cut-off for determining the oligomer content to account for the comparatively high mass of the polymer relative to molecular size.) Additional GPC analyses have been conducted on samples of the polymer produced by the slightly modified process described in Attachment 2 of FCN 885. These analyses indicate an oligomer content below 2000 Daltons of approximately (b)(4) by weight of polymer solids. See **Attachment 1** for details of analyses conducted to determine the low molecular weight oligomer content.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☐ Repeat Use

The FCS copolymer is intended for use as an oil and grease resistant treatment for paper and paperboard used in contact with food. The polymer is currently cleared under FCN 885 for use either in the wet-end or at the size press at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper. The treated paper may contact all types of food under Conditions of Use B through H and in susceptor microwave applications. The food-contact substance is intended for single-service use.

The purpose of this notification is to expand the existing clearance for the FCS polymer to permit its use prior to sheet formation, *e.g.*, in the wet-end of paper production, at levels up to 0.8 wt.% of polymer solids by weight of the paper. No change to the usage rate for size press applications is proposed; however, as discussed in more detail herein, a change is proposed in the language used to describe the intended use. Specifically, the notifier now requests that the language "after sheet formation" be used rather than "size press" applications. All other aspects of the clearance afforded by FCN 885 will remain unchanged.

Suggested language for listing this FCN on FDA's "Inventory of Effective Food Contact Substance Notifications" is set forth in **Attachment 5**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
The FCS will be used prior to sheet formation to treat paper at levels not to exceed 0.8 wt.% of polymer solids by weight of the paper. The FCS will be used after sheet formation to treat paper at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper.	All types of food (Types I through IX)	Conditions of Use B through H and susceptor microwave applications

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

(b)(4) CONFIDENTIAL is intended to impart oil and grease resistance to paper and paperboard used in food-contact applications. Information demonstrating the functionality of the product in such applications was presented in Section II.D.3 and Attachment 15 of FCN 885.

Since FCN 885 became effective, some of the Notifier's customers have determined that to meet the aggressive grease resistance requirements for some particularly demanding applications, a higher loading level of FCS polymer may be needed. As these customers typically apply the FCS prior to sheet formation, *i.e.*, in the wet-end of paper production, the need for the higher treatment level is relevant only to the wet-end use of the polymer.

To illustrate this need, test data are provided with respect to the level of FCS polymer needed in pet food packaging, a typical application for grease-resistance agents. The test method involves placing a test paper sample directly over a standard grid paper. Pet food is then placed on top of the test paper sample and heated in an oven for 24 hours at 140ºC with a 1 kg weight placed on top of the pet food. After 24 hours, the samples are removed from the oven. The pet food and test paper samples are separated from the underlying grid paper and the percentage of stained area on the grid paper is recorded. Acceptable performance requires that when treated paper is exposed to six representative pet foods under these standard conditions, less than 5% staining of the treated paper must be achieved for all six samples.

In testing conducted on the FCS at a dosage level of 12.62 pounds of polymer solids per ton of paper, acceptable performance was reached for five out of six pet foods. See **Attachment 6.** Slightly higher dosages would likely be needed to consistently achieve performance and satisfy the requirements for all samples. Based on these results, a maximum treatment level of 16 lb of polymer solids per ton of paper, or 0.8% polymer solids by weight of paper, is expected to provide adequate grease protection on a consistent basis.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

Please see Section II.E.1 of FCN 885 for information concerning the stability of the FCS polymer. As shown there, the polymer is stable under the intended conditions of use.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II – CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

Please see Section II.E.2 of FCN 885 for relevant information.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration testing has not been carried out. Instead, worst-case migration of FCS oligomers and potential impurities has been calculated based on measured levels in the FCS product and/or in the finished paper. See **Attachment** 7 for details of these calculations.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
N/A					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

No migration testing has been conducted, as stated previously. However, the analyses conducted to determine residual levels of impurities in the FCS and in the finished treated paper were validated in accordance with FDA recommendations. Full details of the method validation experiments are provided in FCN 885.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

Due to space limitations, the worst-case migration calculations are set forth in **Attachment** 7.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The worst-case migration levels calculated in **Attachment** 7 may be multiplied by the applicable consumption factors (CFs) to calculate the corresponding concentrations at which FCS components may enter the diet. Because separate migration levels are calculated in **Attachment** 7 for the use of the FCS under Conditions of B through H and in susceptor microwave applications, separate dietary concentrations are calculated for these two applications. For food-contact applications under Conditions of Use B through H, we use the CF of 0.05 that has been established previously for grease-proofing agents for paper and paperboard. For susceptor microwave applications, we apply the CF of 0.001 that FDA has established for these materials. See **Attachment 8** for these calculations.

For each component, the two separate dietary concentrations calculated for Conditions of Use B-H and microwave susceptors may be summed to calculate the total dietary concentration. The total values thus calculated are shown in Section II.G.3 below. Note that migration and dietary concentration levels are shown in Section II.G.3 for oligomers of the FCS polymer and for only those few impurities for which dietary exposure may increase as a result of this notification. See **Attachment** 7 for a full explanation of the impact of this notification on the dietary concentrations for impurities of the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
FCS Oligomers	--	See Attachment 8	0.14	0.00042	
(b)(4)			0.13	0.00038	
			0.14	0.00041	
			0.28	0.00084	

CONFIDENTIAL

Memorandum

Date November 30, 2010

From Division of Food Contact Notifications
Chemistry Review Team II

Subject FCN 001027 - Keller & Heckman/DuPont Chemicals and Fluoroproducts. Submissions dated 9-10-10 (received 9-14-10) and 11-4-10. Use of perfluoroalkylethyl methacrylate copolymer as a greaseproofing agent in food-contact paper and paperboard.

To Division of Food Contact Notifications
Regulatory Team 2
Attn: P. Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of DuPont Chemicals and Fluoroproducts (DuPont) submitted this Food Contact Notification 1027 (FCN 001027) for the use of the food contact substance (FCS), 2-propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2-propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate, at levels not to exceed 0.8 percent by weight prior to sheet formation and 0.42 percent by weight after sheet formation of dry paper and paperboard intended for use in contact with all food types under Conditions of Use B through H, and in microwave heat-susceptor packaging.

This FCN expands the use of the FCS that is the subject of the effective FCN 885, also submitted by K&H on behalf of DuPont; as such, the notifier notes that this use of the FCN may substitute for the use of the FCS in FCN 885, but not replace it. The submission contains no new information on the identity, manufacturing, or residuals data. We will rely on our final review of FCN 885 *in lieu* of repetition and focus on the differences from FCN 885 in this review.[1] The chemistry review for FCN 885 is attached to this memorandum.

Identity

The identity information is unchanged since our FCN 885 review with the exception of the molecular weight distributions of the FCS. As a result of the manufacturing modifications, as outlined in the Manufacture section below, the molecular weight distributions of the FCS have changed as follows.

Molecular weight data were set forth in Attachment 2 of FCN 885. Analysis of three representative samples of that polymer by size exclusion chromatography (SEC) indicated

[1]See our chemistry memorandum dated 5-14-09 from S. Elyashiv-Barad to P. Honigfort concerning FCN 885, which is attached to this memorandum.

weight-average molecular weights (Mw) of approximately 1.6 million, 1.8 million, and 577,000 Da, and number-average molecular weights (Mn) of approximately 80,000, 92,000, and 83,000 Da. Additional molecular weight data are set forth in Attachment 1 of this FCN. The new data were generated on samples produced by means of the slightly modified manufacturing process presented in this FCN. The analytical methodology is the same as that used in the testing described in Attachment 2 of FCN 885. As shown in Attachment 1 of this FCN, the new analyses indicated Mw values of approximately 2.2 million and 2.6 million, and Mn values of 170,000 and 133,000 Da.

Manufacture

The manufacturing process for the FCS was described in Attachment 4 of FCN 885. Some minor changes in the process are described in Attachment 2 of this notification. This version of the FCS is equivalent to the previous version outlined in FCN 885; i.e., the monomers and their ratios are identical. However, slight changes to the manufacture process have been made to allow for the product to be manufactured at higher solids and in different kettle set arrangements.

(b)(4)

Impurities

A full impurity profile for the FCS was provided in FCN 885. Additional analyses have been
conducted on the current FCS on lots that were produced by the slightly modified manufacturing process described above (see Attachment 3 of this FCN for a tabulation of the impurity concentrations measured in these samples). The analytical methods used to determine impurities in the FCS were fully described in FCN 885 (see Attachments 6-11 of FCN 885 for the analytical methodology and validation of the test methods). Raw data from the new analyses, including peak integrations and representative chromatograms or other instrument output, are presented in Attachment 4 of this FCN.

Intended Use and Technical Effect

This FCN seeks to increase the use level to 0.8% by weight of the paper when used prior to the sheet forming process, roughly double the use level of 0.42% when applied after the sheet
forming process as described in FCN 885.

As K&H explain, since FCN 885 became effective, some of DuPont's customers have determined that to meet the aggressive grease resistance requirements for some particularly demanding applications (specifically pet food bags), a higher loading level of FCS polymer may be needed. As these customers typically apply the FCS prior to sheet formation, i.e., in the wet-end of paper production, the need for the higher treatment level is relevant only to the wet-end use of the polymer. Efficacy data are included in Attachment 6. Also, see our review of FCN 885 for more technical effect information.

Stability

See our FCN 885 review for stability information.

Migration Studies

Migration testing has not been carried out. Instead, worst-case 100% migration of FCS oligomers and potential impurities has been calculated based on measured levels in the FCS product and/or in the finished paper. Attachment 7 shows the details of these calculations.

Worst-case migration of FCS oligomers was calculated in Attachment 18 of FCN 885 by assuming 100% migration from treated paper to food. Based on data presented in FCN 885, the low molecular weight (LMW) oligomer content was estimated to be 0.045% by weight of the polymer. Using this value, together with the maximum treatment level of 0.42 wt.% and the standard assumptions noted above, worst-case oligomer migration levels of 9.5 ppb for paper and paperboard used under Conditions of Use B-H and 8.7 ppb for paper used in susceptor microwave applications were calculated in FCN 885.

This FCN proposes to increase the maximum treatment level from 0.42 wt.% to 0.8 wt.% when the FCS polymer is applied prior to sheet-forming (i.e., in the wet end). For purposes of migration calculations specific to wet-end use of the FCS, K&H assumed that 100% of the FCS oligomers are incorporated into the finished paper and that 100% of the oligomers will migrate to food. Thus, the calculations are the same as those presented in FCN 885 except for the higher treatment level.

Data submitted in Attachment 1 of this FCN indicate an oligomer content of approximately 0.012% by weight of the polymer for samples of the polymer produced by the modified process described. The oligomer content of 0.045 wt. % established in FCN 885 was based on analysis of a single commercial production batch; as discussed in FCN 885, after that lot was produced, the process was modified slightly to achieve higher molecular weight, primarily by reducing the amount of initiator used. To account for these changes as well as the additional process changes described in this FCN, they rely in this submission on the low molecular weight oligomer content of 0.012 wt.%, as this was determined on more recent pilot production that reflects the various process changes.

Typically, migration calculations for impurities of wet-end additives rely on the assumption that no more than about 2% of the total quantity of non-substantive impurities present will be incorporated into the paper.[2] By contrast, for additives applied to the paper sheet at the size press, it is assumed that 100% of the impurities present in the additive are incorporated into the treated paper. Consequently, for additives applied at the same level at either the size press or in the wet end, the worst-case migration level calculated for impurities is typically 50 times higher when the additive is applied at the size press than when the additive is applied at the wet end.

This being the case, and considering that worst-case migration of FCS impurities was determined in FCN 885 based entirely on the use of the FCS at the size press, where the impurities will be incorporated into the paper sheet to the greatest extent, no increase in potential migration of impurities will occur as a result of the use of the FCS at the proposed higher level of 0.8 wt.% at the wet-end. While this represents an approximate doubling of the treatment level in those cases in which the FCS is applied at the wet-end, the migration level that would be calculated for this treatment level will still remain below the migration level calculated in FCN 885 based on the polymer being applied at the 0.42 wt.% level at the size press or at any other point after sheet formation. K&H include a detailed calculation to show that exposure to impurities from the wet end process would be insignificant when compared to the sheet forming process as determined in FCN 885. We concur with their assessment that this new use of the FCS will not alter exposure to the impurities, except for a

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[2]In footnote 2 of their Attachment 7, K&H calculate that 5 g of pulp in the original slurry would become 5 g of pulp in 15 g of wet paper, using our standard assumptions (33% pulp). That means 985 g of white water (containing the non-substantive impurities) would be removed. Only 10 g of the original 985 g would be present, or ~1% , clearly < 2% as claimed.

few discussed in Attachment 7.

Impurities that do appear to be present at higher concentrations in lots made by the modified process include the (b)(4) The following table compares the concentrations of these impurities found in the samples analyzed in FCN 885 and in this FCN:

Table 1. Comparison of Concentrations of Impurities Found in FCS Samples Analyzed in FCNs 885 and 1027

Compound	Plant Batch 2	E336 Pilot D10050-110	E336 Pilot D10050-11
(b)(4)	389 ppm	716 ppm	778 ppm
	397 ppm	702 ppm	810 ppm
	29 ppm	79 ppm	32 ppm
	1150 ppm	6650 ppm	3520 ppm

DuPont believes that the higher residual solvent concentrations found in the E336 pilot batches is an artifact of the pilot production process, in which the product may not be distilled to the same extent as in commercial production. As a result, the end product may contain higher levels of residual solvents than would be found in a commercial batch. The higher levels of (b)(4) likely result from the same phenomenon. To ensure that the worst-case calculated migration levels adequately account for the levels of residual impurities to be found in the FCS, they have conservatively treated the E336 pilot lot samples as if they are fully representative of the commercial production process. They have
adjusted the migration levels previously calculated in FCN 885 to reflect the higher residual levels shown in the table above.

Exposure

For the oligomers, as discussed in Attachment 7, K&H assumed 100% migration to fatty food (4.8 ppb) under Conditions of Use B through H and have calculated migration to aqueous food (1.2 ppb) based on previously submitted migration data. The calculations are as follows:

$$\langle M \rangle = (1.2 \text{ ppb} \times 0.59) + (4.8 \text{ ppb} \times 0.41) = 2.68 \text{ ppb}$$

$$\text{Dietary Concentration (DC)} = \langle M \rangle \times CF = 2.68 \text{ ppb} \times 0.05 = 0.13 \text{ ppb}$$

For microwave susceptor applications, we will multiply the worst-case migration level (4.4 ppb) by the CF of 0.001:

DC = 4.4 ppb x 0.001 = 0.0044 ppb

The total DC for oligomers is the sum of the two calculated values, or ~ 0.14 ppb.

The calculated dietary concentration is lower than the DC calculated in FCN 885 (0.28 ppb), despite the fact that this FCN proposes a higher maximum application rate when the FCS is applied at the wet-end of paper production. This is because the GPC data submitted in this notification indicate a lower content of LMW oligomers than the level measured in FCN 885.

The only *new* exposure estimates from this FCN are for the oligomers, (b)(4) Their DCs are summarized in the following table:

Table 2. New Exposure to Oligomers, and Impurities from the Expanded Use of the FCS

Compound	DC[3]	EDI[4]
oligomers	0.14 ppb	0.42 µg/p/d
(b)(4)	0.14 ppb	0.42 µg/p/d
	0.13 ppb	0.39 µg/p/d
	0.28 ppb	0.84 µg/p/d

As we noted in our FCN 885 review, "We concur with the notifier's approach and with the notifier's exposure estimates." We have attached the entire chemistry review which contains all the exposure estimates.

Cumulative Exposure (CEDI)

(b)(4) is a common industrial solvent. The exposure to (b)(4) of 0.28 ppb in the diet is expected to be an insignificant addition to its CEDI.

The exposure to (b)(4) from the proposed use of the FCS is 0.13 ppb in the diet. This exposure subsumes the exposure to (b)(4) from the use of the FCS in FCN 885. The highest exposure to (b)(4) from all similar

[3]We note that all of these DCs are an increase over the DCs calculated for the use of the FCS in FCN 885, with the exception of the oligomers. As stated previously, this is because the GPC data submitted in this notification indicate a lower content of LMW oligomers (0.12 wt-%) than the level measured (0.045 wt-%) in FCN 885.

[4]The estimated daily intake (EDI) is calculated by multiplying the DC by a daily diet of 3000 g food/person/day.

greaseproofing agents, which would substitute for each other, is found for the effective use of the FCS in FCN (b)(4) and is calculated to be 2.3 ppb in the diet (see our chemistry memorandum dated 12-1-09 concerning FCN (b)(4)). Therefore, there will be no increase in exposure to (b)(4) from the proposed use of the FCS.

The exposure to (b)(4)) from the proposed use of the FCS is 0.14 ppb in the diet. This exposure subsumes the exposure to (b)(4) from the use of the FCS in FCN 885. The highest exposure to (b)(4) from all similar greaseproofing agents, which would substitute for each other, is found for the effective use of the FCS in FCN (b)(4) and is calculated to be 0.58 ppb in the diet (see our chemistry memorandum dated 2-19-10 concerning FCN (b)(4)). Therefore, there will be no increase in exposure to (b)(4) from the proposed use of the FCS.

The exposure to the oligomers and other impurities for the proposed use of the FCS are subsumed by their exposures as calculated in FCN (b)(4) Therefore, there is no increase in the CEDI to these compounds.

Notification Language

The notification language, as presented in your acknowledgment letter dated 10-6-10, is appropriate as written.

Roseann M. Costantino, Ph. D.

HFS-275 (R/F)
HFS-275:RMCostantino:FCN 001037.wpd: 11-22-10
R/DInit:HFS-275:MAAdams:11-30-10
Final:maa: 11-30-10

(b) (5)

DAIKIN AMERICA FCN 820

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-methyl-, polymer with 2-(diethylamino)ethyl 2-methyl-2-propenoate, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-methyl-2-propenoate, acetate

2. CAS Registry Number

1071022-26-8

3. Trade or Common Name

(b)(4) **CONFIDENTIAL**

4. Other Chemical Names *(IUPAC, etc*

Acetate salts of methacrylic acid copolymer with acrylic acid, diethylaminoethyl methacrylate, and 2-(perfluorohexyl)ethyl methacrylate

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is fully described in FCN 885. For ready reference, the basic descriptive information set forth in Part II, Section A.5 of FCN 885 is reproduced below.

The starting monomers used in the manufacture of the FCS are as follows:

(b)(4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Representative IR and NMR (^{1}H and ^{13}C) spectra are provided in Attachment 3 of FCN 885.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†

Information on the substances used in the manufacture of the FCS is provided in FCN 885 and is incorporated by reference. Please see **Attachment 2** of this FCN for additional information.

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

The manufacturing process for the FCS was described in Attachment 4 of FCN 885. Some minor changes in the process are described in **Attachment 2** of this notification.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
See **Attachment 3**				

A full impurity profile for the FCS was provided in FCN 885. Additional analyses have been conducted on FCS lots that were produced by the slightly modified manufacturing process described in **Attachment 2** of this notification. Please see **Attachment 3** for a tabulation of the impurity concentrations measured in these samples. The analytical methods used to determine impurities in the FCS were fully described in FCN 885; please see Attachments 6-11 of FCN 885 for the analytical methodology and validation of the test methods. Raw data from the new analyses, including peak integrations and representative chromatograms or other instrument output, are set forth in a supplemental report presented in **Attachment 4**.

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
N/A	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES

(b)(4) [redacted]

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

GPC analyses presented in FCN 885 indicated a low molecular weight oligomer (LMWO) content below 2000 Daltons of (b)(4) by weight of polymer solids. (Due to the fluorinated nature of the polymer, we have used 2000 Daltons rather than 1000 Daltons as the upper cut-off for determining the oligomer content to account for the comparatively high mass of the polymer relative to molecular size.) Additional GPC analyses have been conducted on samples of the polymer produced by the slightly modified process described in Attachment 2 of FCN 885. These analyses indicate an oligomer content below 2000 Daltons of approximately (b)(4) by weight of polymer solids. See **Attachment 1** for details of analyses conducted to determine the low molecular weight oligomer content.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☐ Repeat Use

The FCS copolymer is intended for use as an oil and grease resistant treatment for paper and paperboard used in contact with food. The polymer is currently cleared under FCN 885 for use either in the wet-end or at the size press at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper. The treated paper may contact all types of food under Conditions of Use B through H and in susceptor microwave applications. The food-contact substance is intended for single-service use.

The purpose of this notification is to expand the existing clearance for the FCS polymer to permit its use prior to sheet formation, *e.g.*, in the wet-end of paper production, at levels up to 0.8 wt.% of polymer solids by weight of the paper. No change to the usage rate for size press applications is proposed; however, as discussed in more detail herein, a change is proposed in the language used to describe the intended use. Specifically, the notifier now requests that the language "after sheet formation" be used rather than "size press" applications. All other aspects of the clearance afforded by FCN 885 will remain unchanged.

Suggested language for listing this FCN on FDA's "Inventory of Effective Food Contact Substance Notifications" is set forth in **Attachment 5**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
The FCS will be used prior to sheet formation to treat paper at levels not to exceed 0.8 wt.% of polymer solids by weight of the paper. The FCS will be used after sheet formation to treat paper at levels not to exceed 0.42 wt.% of polymer solids by weight of the paper.	All types of food (Types I through IX)	Conditions of Use B through H and susceptor microwave applications

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

(b)(4) CONFIDENTIAL is intended to impart oil and grease resistance to paper and paperboard used in food-contact applications. Information demonstrating the functionality of the product in such applications was presented in Section II.D.3 and Attachment 15 of FCN 885.

Since FCN 885 became effective, some of the Notifier's customers have determined that to meet the aggressive grease resistance requirements for some particularly demanding applications, a higher loading level of FCS polymer may be needed. As these customers typically apply the FCS prior to sheet formation, *i.e.*, in the wet-end of paper production, the need for the higher treatment level is relevant only to the wet-end use of the polymer.

To illustrate this need, test data are provided with respect to the level of FCS polymer needed in pet food packaging, a typical application for grease-resistance agents. The test method involves placing a test paper sample directly over a standard grid paper. Pet food is then placed on top of the test paper sample and heated in an oven for 24 hours at 140ºC with a 1 kg weight placed on top of the pet food. After 24 hours, the samples are removed from the oven. The pet food and test paper samples are separated from the underlying grid paper and the percentage of stained area on the grid paper is recorded. Acceptable performance requires that when treated paper is exposed to six representative pet foods under these standard conditions, less than 5% staining of the treated paper must be achieved for all six samples.

In testing conducted on the FCS at a dosage level of 12.62 pounds of polymer solids per ton of paper, acceptable performance was reached for five out of six pet foods. See **Attachment 6.** Slightly higher dosages would likely be needed to consistently achieve performance and satisfy the requirements for all samples. Based on these results, a maximum treatment level of 16 lb of polymer solids per ton of paper, or 0.8% polymer solids by weight of paper, is expected to provide adequate grease protection on a consistent basis.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

Please see Section II.E.1 of FCN 885 for information concerning the stability of the FCS polymer. As shown there, the polymer is stable under the intended conditions of use.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II – CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
Please see Section II.E.2 of FCN 885 for relevant information.			

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration testing has not been carried out. Instead, worst-case migration of FCS oligomers and potential impurities has been calculated based on measured levels in the FCS product and/or in the finished paper. See **Attachment** 7 for details of these calculations.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
N/A					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

No migration testing has been conducted, as stated previously. However, the analyses conducted to determine residual levels of impurities in the FCS and in the finished treated paper were validated in accordance with FDA recommendations. Full details of the method validation experiments are provided in FCN 885.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

Due to space limitations, the worst-case migration calculations are set forth in **Attachment** 7.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The worst-case migration levels calculated in **Attachment** 7 may be multiplied by the applicable consumption factors (CFs) to calculate the corresponding concentrations at which FCS components may enter the diet. Because separate migration levels are calculated in **Attachment** 7 for the use of the FCS under Conditions of B through H and in susceptor microwave applications, separate dietary concentrations are calculated for these two applications. For food-contact applications under Conditions of Use B through H, we use the CF of 0.05 that has been established previously for grease-proofing agents for paper and paperboard. For susceptor microwave applications, we apply the CF of 0.001 that FDA has established for these materials. See **Attachment 8** for these calculations.

For each component, the two separate dietary concentrations calculated for Conditions of Use B-H and microwave susceptors may be summed to calculate the total dietary concentration. The total values thus calculated are shown in Section II.G.3 below. Note that migration and dietary concentration levels are shown in Section II.G.3 for oligomers of the FCS polymer and for only those few impurities for which dietary exposure may increase as a result of this notification. See **Attachment** 7 for a full explanation of the impact of this notification on the dietary concentrations for impurities of the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

N/A

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
FCS Oligomers	--	See Attachment 8	0.14	0.00042	
(b)(4)			0.13	0.00038	
			0.14	0.00041	
			0.28	0.00084	

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Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl)

2. CAS Registry Number

3. Trade or Common Name

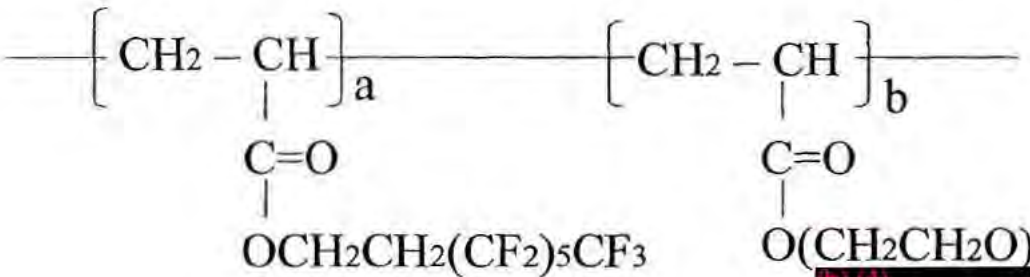
(b) (4) [redacted]

4. Other Chemical Names *(IUPAC, etc.)*

Perfluorohexylethyl acrylate-polyethylene glycol monoacrylate copolymer

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



(b) (4) [redacted]

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Relative monomer weight percentages: (b) (4) [redacted]

(b) (4) [redacted]

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

An IR spectrum of the FCS is available in Attachment 2.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
Perfluorohexylethyl acrylate (13FA)	17527-29-6	Monomer	☒ Yes ☐ No
Polyethylene glycol monoacrylate (PEG-monoacrylate)	26403-58-7	Monomer	☒ Yes ☐ No
(b) (4) [redacted]			
			☐ Yes ☐ No
• See Attachment 3 for Certificates of Analysis for reagents			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See Attachment 4 for the CONFIDENTIAL manufacturing process diagram and the CONFIDENTIAL reaction pathway diagram for the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including. the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
Perfluorohexylethyl acrylate (13FA)	17527-29-6	<50 ppm	CONFIDENTIAL	☒ Yes ☐ No
Polyethylene glycol monoacrylate (PEG-monoacrylate)	26403-58-7	133 ppm		☒ Yes ☐ No
[redacted]		<1000 ppm		☒ Yes ☐ No
		50 ppm		☒ Yes ☐ No
		<20 ppm		☒ Yes ☐ No
		45 ppb		☒ Yes ☐ No
		23 ppb		☒ Yes ☐ No
		248 ppm		☒ Yes ☐ No
		<5000 ppm		☒ Yes ☐ No
		<80 ppm		☒ Yes ☐ No
		<100 ppm		☒ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

- For test results from residuals testing, see Attachments 5 and 6.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
Solids Content (%) (b) (4)	(b) (4)
pH (25°C) (b) (4)	
Specific Gravity (b) (4)	
Remaining solvent (%) (b) (4)	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Mw/Mn (See Attachment 7)			(b) (4)
Tg (See Attachment 8)			

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

The percentage of the FCS with a MW <1000 daltons is approximately 0.5%. See Attachment 7 for supporting SEC data.

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☒ Repeat Use

The polymer additive is intended to be used in paper and paperboard at a level not to exceed 0.2% dry weight. Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS may be applied at the size press or the wet end.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
As a polymer additive in paper and paperboard at a level not to exceed 0.2% dry weight.	All food types as described in Table 1 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html.	Conditions of Use A-H as described in Table 2 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

As stated above, the polymer additive is intended to be used in paper and paperboard at a level not to exceed 0.2% dry weight. Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS may be applied at the size press or the wet end.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 10 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 10 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

The FCS imparts grease and oil resistance to paper and paperboard. Test results demonstrating this technical effect can be found in Attachment 9.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

No degradation of the FCS is anticipated during consumer use of paper or paperboard coated with the fluoropolymer. The results of thermogravimetric analysis on the FCS, which demonstrates its stability under proposed conditions of use, can be found in Attachment 10.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
(b) (4)			

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D 5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Not applicable – no migration testing was done for this FCS. See section II.F.2. of this form for a discussion of residual analyses that were done on the FCS. Exposure estimates were then conducted based on 100% migration of the residual level into food.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Not applicable.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable. *See* report of The National Food Laboratory for residual analyses in the dried polymer and validation of these analyses.

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2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

A sample of the FCS was tested for residual monomers, oligomers, and for the presence of potential impurities. The CONFIDENTIAL composition of the test material can be found in Attachment 11.

The fluoropolymer was dissolved in acetone, and the resulting solution was analyzed by GC/MS for the monomers, (b) (4) were determined by a different laboratory using LC-MS. Residual amounts detected are provided in table II.B.3. of this form. Exposure estimates based on 100% migration of residuals are provided in Attachment 12. An example calculation, for 13FA follows:

Residual 13FA Monomer

1. The polymer is used at 0.2% in paper. (The product containing the polymer is used at 1.0%.)
2. The basis weight of paper is 0.050 g/in^2
3. Migration from paper to food is 100%
4. 10 g of food will contact each square inch of paper

The average residual level of 13FA monomer is <50 parts per million (ppm or μg/g). Assuming 100% of the 13FA will migrate to food:

[(50 $\mu g_{13FA}/g_{polymer}$) x (0.05g_{paper}/in^2) x (0.2 $g_{polymer}/g_{solution}$) x (0.01 $g_{solution}/g_{paper}$)] ÷ 10g_{food}/in^2 = 0.0005 $\mu g_{13FA}/g_{food}$ ≡ 0.5 ppb

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See Attachment 12 for dietary concentration calculations for residual materials in the fluoropolymer FCS. As above, an example calculation, for 13FA follows:

Given a CF of 0.05 for specialty paper, the dietary concentration for 13FA is

0.5 ppb x 5% CF = 0.025 ppb, or 0.025 µg/kg

The EDI is 0.025 µg/kg x 3 kg/p/d = 0.075 µg/p/d

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 10 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 10 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Perfluorohexylethyl acrylate (13FA)	17527-29-6		0.025 ppb	0.075 µg/p/d	
Polyethylene glycol monoacrylate (PEG-monoacrylate)	26403-58-7		0.067 ppb	0.20 µg/p/d	
(b) (4) [redacted]			0.125 ppb	0.375 µg/p/d	
			2.5 ppb	7.5 µg/p/d	
			0.5 ppb	1.5 µg/p/d	
			0.025 ppb	0.075 µg/p/d	
			0.01 ppb	0.03 µg/p/d	
			0.0225 ppt	0.0675 ng/p/d	
			0.0125 ppt	0.0375 ng/p/d	
			0.8 ppb	2.4 µg/p/d	
			1 ppb	3 µg/p/d	
FCS Oligomers <1000 Daltons			2.5 ppb	7.5 µg/p/d	
FCS Oligomers <1600 Daltons			8.5 ppb	25.5 µg/p/d	

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Hepp, Mark A

From: Hill, Devon W. [Hill@khlaw.com]
Sent: Thursday, June 05, 2008 2:07 PM
To: Hepp, Mark A
Cc: Starosta, Kelly R.
Subject: RE: FCN 820
Attachments: Response to FDA's 5-21-08 Letter (redacted).pdf; Response to FDA's 5-21-08 Letter.pdf

Dr. Hepp, please see our response to your letter of May 21, 2008 in regard to FDA's evaluation of FCN 820.

My best, Devon

From: Hepp, Mark A [mailto:mark.hepp@fda.hhs.gov]
Sent: Wednesday, May 21, 2008 4:25 PM
To: Hill, Devon W.
Subject: FCN 820

As we discussed by telephone.
If you have any questions, please do not hesitate to contact me.

Best regards,

Mark Hepp

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June 5, 2008

Via Electronic Mail and Federal Express

Mark Hepp, Ph.D.
Division of Food Contact Notifications
Food and Drug Administration
Office of Food Additive Safety (HFS-275)
Center for Food Safety and Applied Nutrition
5100 Paint Branch Parkway
College Park, Maryland 20740

Re: Daikin America, Inc.; FCN 820; Response to FDA's May 21, 2008 Letter; Our File No. (b) (4) [redacted]

Dear Dr. Hepp:

On behalf of our client, Daikin America, Inc. the purpose of this letter is to respond to the Food and Drug Administration's (FDA) May 21, 2008 letter requesting additional information for Food-Contact Notification (FCN) 820. FCN 820 was received by FDA on April 1, 2008, and proposed the use of 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl) to impart grease and oil resistance to paper and paperboard. In this letter, we have provided a full response to each of FDA's questions in the May 21, 2008 letter. With regard to FDA's concerns regarding bioaccumulation and the dietary exposure to the oligomers of the food-contact substance (FCS), which we believe is the most significant question in FDA's letter, (b) (4) [redacted] FDA's other questions identified in your May 21, 2008 letter are addressed in turn below.

Please note that we have marked some information in this letter and its attachments as "CONFIDENTIAL," and have enclosed a redacted copy for your use in responding to Freedom of Information Act (FOIA) requests.

For ease of reference, we repeat below the questions from your May 21, 2008 letter (some questions are abbreviated), followed by our responses.

1. *Your notification identifies* (b) (4) [redacted] *as components of the finished food-contact substance, but does not describe*

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their use as part of the manufacturing process. Please explain the presence of these two compounds in the food-contact substance and, if used in the manufacturing process, please provide information on the quantities used.

(b) (4) are not part of the manufacturing process for the FCS; however, these materials could be present, at very low levels, as impurities in the FCS because of their presence in the starting monomers. (b) (4) are not intentionally added by Daikin. More specifically, (b) (4) is added as a stabilizer for the 13FA monomer by the manufacturer of the monomer. Likewise, (b) (4) is added as a stabilizer to both the 13FA and PEG-monoacrylate monomers by the manufacturer of those starting materials. Neither (b) (4) is intended to serve any technical effect in the finished FCS. However, residual levels of these substances may nonetheless be present as impurities in the finished FCS and, as such, they were identified in our notification and the potential exposure to these substances was addressed.

2. *Attachment 6 of your notification contains data supporting the analysis of the food-contact substance for* (b) (4) (b) (4) *including sample chromatograms and mass spectra. However, your notification does not contain the raw data for the analyses (peak areas for analytes) or the calibration data. Please provide calibration data demonstrating the linearity of the method, and the appropriate supporting data for these plots (standard concentrations, sample chromatograms, peak areas, etc.).*

Please see the attached supplement to the (b) (4) (b) (4) analysis report (Attachment 1), originally submitted as Attachment 6 of FCN 820. Included in this supplement are peak area data for the lowest calibration standard, a blank sample, and three lots of the FCS. The data from these analyses of residual (b) (4) in the FCS are used to calculate worst-case dietary concentrations of 0.0225 parts per trillion (ppt) and 0.0125 ppt, respectively, assuming 100% migration of residual (b) (4) from the FCS into food. This worst-case dietary concentration of (b) (4) yields in a risk value of 1.25×10^{-11}, which is considered negligible. Even at residual concentrations several orders of magnitude higher than what are detected in the FCS, neither impurity would present a risk to human health and safety.

3. *We tentatively estimate the potential human exposure to the low molecular weight oligomeric fraction of your polymer to be 27 µg per person per day, in agreement with the analysis you provided in your notification.*

. . . .

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(b) (4)

. . . .

(b) (4)

(b) (4)

(b) (4)

(b) (4)

[redacted]

4. Finally, your submission contained a claim, under Title 21 C.F.R. 25.32(i), that the action of permitting your food-contact substance notification to become effective is among the classes of actions that are ordinarily excluded from the requirement of preparing either an environmental assessment or an environmental impact statement. Title 21 C.F.R. 25.32(i) excludes food-contact substance notifications from this requirement when the substance that is the subject of the notification is present in the finished food packaging material at no greater than five percent by weight and it expected to remain with the finished food packaging materials through use by consumers.

(b) (4)

[redacted]

(b) (4)

[redacted]

(b) (4) [redacted]

(b) (4) [redacted]

the FCS prior to sheet formation, and we are amending our request to only cover the use of the polymer when added at the size press. As we now only seek application of the FCS at the size press, (b) (4) [redacted] longer relevant. We do not believe that any further information is needed to support the categorical exclusion from the need to prepare an environmental assessment for applications that only involve the application of the FCS at the size press.

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* * *

We hope that you will find these answers fully responsive to your questions so that FCN 820 is considered complete. Should you have any additional questions, however, please do not hesitate to contact us, preferably by e-mail or telephone, so that we may respond as quickly as possible. Thank you for your assistance in this matter.

Sincerely yours,

(b) (6) [redacted]

Devon Wm. Hill

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: July 1, 2008

From: Division of Food Contact Notifications
Chemistry Team 2

Subject: FCN 820: Use of 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl) as a grease-proofing agent for food-contact paper and paperboard.

To: Division of Food Contact Notifications
Regulatory Team 1
Attn: M. Hepp, Ph.D

Daikin America, through Keller and Heckman, L.L.C., submitted this food-contact notification (FCN 820) for the use of 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl) as a grease-proofing agent for food-contact paper and paperboard. The food-contact substance (FCS) will be used at a level not to exceed 0.2% of the finished food-contact paper and paperboard.

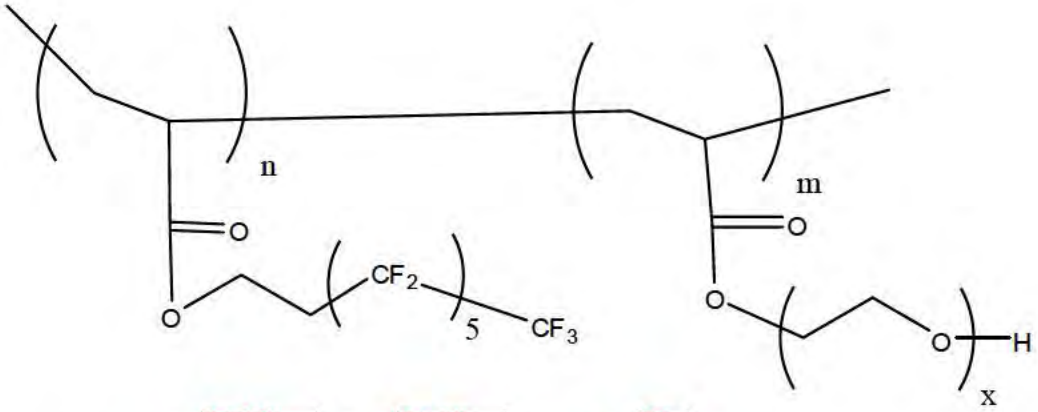
Regulatory Status

The FCS is not currently regulated or authorized for use in contact with food. There are numerous perfluoro-based grease-proofing agents regulated or authorized for use in contact with food. The FCSs described in FCNs 628, 604, 599, 338, 311, and 206 are prepared from the same or similar perfluoroalkylethylacrylate monomers. A second FCN (FCN 827) was submitted by Daikin America for a very similar material containing the additional monomers 1-propenoic acid, 2-hydroxyethyl ester and polyethylene glycol diacrylate.

Identity

CAS Name:	2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl)
CAS Numbers:	Not provided
Other Names:	perfluorohexylethylacrylate-polyethylene glycol monoacrylate copolymer
Trade Name:	(b) (4) [redacted]
Molecular Weight:	Mn = (b) (4) [redacted] Mw = (b) (4) [redacted]

Structure:



n = (b) (4) m = (b) (4) average x (b) (4)

Characterization

The notifier proved in Attachments 2 of the FCN an IR spectrum of the FCS. The spectrum is consistent with the structure of the FCS.

Manufacture

The notifier provided a detailed description of the manufacture of the FCS in Attachment 4 of the FCN. The notifier stated that (b) (4) are present in the finished FCS but the manufacturing section of the FCN does not provide details as to their purpose in the FCS or the quantities used in the manufacturing process. The notifier stated in the 6/5/2008 updated to the notification that these materials are antioxidants/stabilizers in the monomers used to prepare the FCS. Both (b) (4) are regulated for their intended use in 21 CFR 176.170 (Components of paper and paperboard in contact with aqueous and fatty foods).

(b) (4)

Intended Use/Use level/Technical effect

The FCS is intended to be used as a grease-proofing agent for food-contact paper and paperboard. The notifier provided data supporting the intended technical effect in Attachment 9 of the FCN. The FCS will be used at a level not to exceed 0.2% of the finished food-contact paper and paperboard. The FCS was intended to be applied at (b) (4) the size press. (b) (4)

Stability

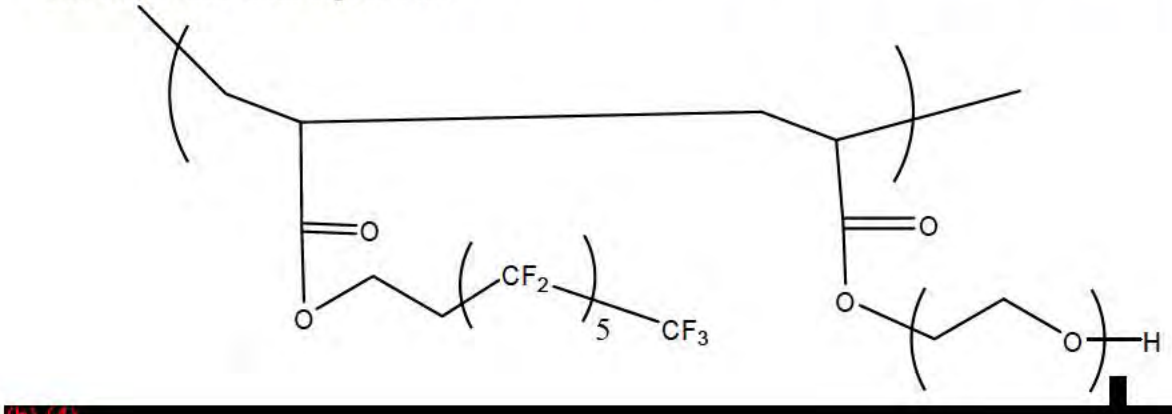
The notifier states that the FCS is stable under the intended conditions of use. The notifier provided a thermogravimetric analysis of the FCS in Attachment 10. The data support the notifier's conclusion that the material is stable under the intended conditions of use.

Migration Testing

Migration testing was not conducted in support of this notification. Instead, the notifier performed residue analyses for impurities in the finished FCS. The notifier performed gel-permeation chromatography (GPC) on the finished FCS to determine the residual level of oligomers in the FCS.

The notifier analyzed three lots of the FCS using gel-permeation chromatography/multiple-angle-laser-light-scattering (MALLS) calibrated with polystyrene standards. Using this method, the notifier determined that there was approximately 1.7 weight-percent oligomers below 1600 Daltons.

For the FCS, Toxicology typically requests that Chemistry calculate exposure to oligomers that have a molecular weight below 1000 Daltons. In reviewing the chemistry memoranda for various FCNs for perfluorinated grease-proofing agents, we note that we have provided toxicology with exposure values based on 1000, 2200 and 2500 Daltons. In addition, there have been a number of discussions regarding the relative size of these perfluorinated oligomers versus their hydrocarbon analogs and how that might affect absorption in the gut. Although chemistry cannot speak to the bioavailability of these perfluorinated species compared to their hydrocarbon analogs, we can provide some insight into their relative size. Using Chem3D Ultra[1] version 6.0, we have determined the solvent-excluded volume and molecular weight of a representative repeat unit in the FCS and the analogous hydrocarbon version of that same repeat unit.



(b) (4)

1 . CambridgeSoft Corp., Cambridge, MA 02140.

The notifier analyzed triplicate samples of the FCS for residual perfluorohexylethylacrylate, polyethylene glycol monoacrylate (b) (4) [redacted] using gas chromatography/mass spectroscopy. The notifier prepared standard solutions of and calibration curves for each analyte. The correlation coefficients for each of the calibration curves are acceptable. Perfluorohexylethylacrylate, (b) (4) [redacted] were not detected in any of the replicate samples of the FCS. These results were validated by spiking samples of the FCS with each of the analytes at their respective limits of detection. All spikes were detected.

The notifier did detect polyethylene glycol monoacrylate (b) (4) [redacted] in the FCS at an average of 133 ppm and 248 ppm, respectively. The results were validated by spiking triplicate samples of the FCS at one-half, one and twice the detected level of the analyte. The average recoveries for polyethylene glycol monoacrylate and (b) (4) [redacted] were 95% and 96%, respectively. All recoveries are acceptable.

The notifier also analyzed multiple samples of the FCS for residual (b) (4) [redacted] using liquid chromatography/mass spectroscopy. (b) (4) [redacted] were detected in the replicate samples of the FCS at a concentration of 10 ppb and 5 ppb, respectively. This is equivalent to 0.045µg/kg and 0.025 µg/kg FCS on a dry-weight basis. These results were validated by spiking samples of the FCS with each of the analytes at 40 µg/L. Although the notifier did not provide all of the supporting data that we typically recommend, the spike and recovery experiment returned acceptable percent recoveries for these analytes. Given the vanishingly small exposures to these materials, the results of the analytical analysis would need to contain gross errors (2-3 orders of magnitude) in order to contribution to their respective cumulative exposures. After evaluation of all analytical data in the notification, we have no reason to assume such errors exist for these measurements. Therefore, we have no concerns for the data on (b) (4) [redacted]

Exposure Estimates

(b) (4) [redacted]

notification. We have evaluated and agree with the notifier's calculation.

Exposures were estimated using the residual levels of the respective impurities or the quantity of oligomers below 1600 Daltons, the maximum requested application rate of the FCS at the size press (0.2%), our standard assumption for average basis weight of all food-contact paper and paperboard (0.05 g/in^2), our standard assumption for the quantity of food in contact with food packaging (10 g/in^2), the assumption of 100% migration to food, and a refined consumption factor of 0.003 (b) (4) [redacted]
The dietary concentrations (DC) and estimated daily intake values are summarized in Table 1. A sample calculation using the oligomers is below.

$$\mathrm{DC} = (0.003)\left(\frac{1.7\ \mathrm{g}}{100\ \mathrm{g\ FCS}}\right)\left(\frac{0.2\ \mathrm{g\ FCS}}{100\ \mathrm{g\ paper}}\right)\left(\frac{0.05\ \mathrm{g\ paper}}{1\ \mathrm{in}^2}\right)\left(\frac{1\ \mathrm{in}^2}{10\ \mathrm{g\ food}}\right)\left(\frac{1000\ \mathrm{g\ food}}{1\ \mathrm{kg\ food}}\right)\left(\frac{1000\ \mathrm{mg}}{1\ \mathrm{g}}\right)\left(\frac{1000\ \mu\mathrm{g}}{1\ \mathrm{mg}}\right) = 0.5\ \mu\mathrm{g/kg\ food}$$

The estimated daily intake (EDI) is calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = (3\ kg\ food/p/d)(0.5\ \mu g/kg\ food) = 1.5\ \mu g/p/d$$

Table 1. Tentative Exposure Estimates

	Residual level	DC (ppb)	EDI (µg/p/d)
FCS (oligomers below 1600 Daltons)	1.7 wt-%	0.5	1.5
13FA monomer	50 µg/g FCS	0.002	0.006
Polyethylene glycol monoacrylate	133 µg/g FCS	0.004	0.01
(b) (4) [redacted]	248 µg/g FCS	0.007	0.02
	1000 µg/g FCS	0.03	0.09
	50 µg/g FCS	0.002	0.006
	20 µg/g FCS	0.0006	0.002
	5000 µg/g FCS	0.2	0.6
	0.009 µg/g FCS	$3x10^{-07}$	$9x10^{-07}$
	0.005 µg/g FCS	$2x10^{-07}$	$6x10^{-07}$
		Regulated	176.170
		Regulated	176.170

Cumulative Exposure Estimates

C6-based perfluoro oligomers

(b) (4) [redacted] As such, there are three effective food contact notifications for perfluoro polymers with side chains containing six perfluorinated carbon atoms (*e.g.,* 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester), FCNs 542, 599 and 604. A review of the chemistry memoranda for FCNs 542, 599, 604 indicates that exposure to C6 oligomers is 0.5 ppb, 0.5 ppb, and 10 pptr, respectively. As these calculations are based on our consumption factor for specialty paper and 100% market capture and the intended uses are considered substitutional, the cumulative DC of the C6 oligomers would be 0.5 ppb. (b) (4) [redacted] we must assume that the exposures would be additive. As such, a conservative estimate for the cumulative DC of the C6 oligomers would be 0.5 ppb from FCNs 542, 599, and 604 plus 0.5 ppb from this FCN, or 1 ppb. However, in all likelihood, this is an overestimate with the actual cumulative DC between 0.5 and 1 ppb. The cumulative EDI of the C6 oligomers is 1.5-3 µg/p/d.

Impurities

Given the vanishingly small EDIs for the impurities, they would not contribute to their

2. The EDI is equivalent to 1.7 x 10^9 molecules or 1.7 billion molecules of PFHA and 1.2 billion molecules of PFOA.

respective CEDIs. Therefore, there will be no change in their cumulative EDIs.

Kirk Arvidson, Ph.D.

HFS-275 (R/F); HFS-705 (Diachenko)
HFS-275: KBArvidson:436-1152:FCN000820_C_MEMO:6/26/2008
R/D Init: MAAdams:7/1/2008
F/T:kba:7/1/2008

EDI of the C6 oligomers is 1.5-3 μg/p/d.

Impurities

Given the vanishingly small EDIs for the impurities, they would not contribute to their respective CEDIs. Therefore, there will be no change in their cumulative EDIs.

(b) (6)

[redacted]

Kirk Arvidson, Ph.D.

HFS-275 (R/F); HFS-705 (Diachenko)
HFS-275: KBArvidson:436-1152:FCN000820_C_MEMO:6/26/2008
R/D Init: MAAdams:7/1/2008
F/T:kba:7/1/2008

DAIKING AMERICA FCN 827

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-hydroxyethyl ester, polymer with α-(1-oxo-2-propen-1-yl)-ω-hydroxypoly(oxy-1,2-ethanediyl), α-(1-oxo-2-propen-1-yl)-ω-[(1-oxo-2-propen-1-yl)oxy]poly(oxy-1,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate

2. CAS Registry Number

1012783-70-8

3. Trade or Common Name

(b) (4) [redacted]

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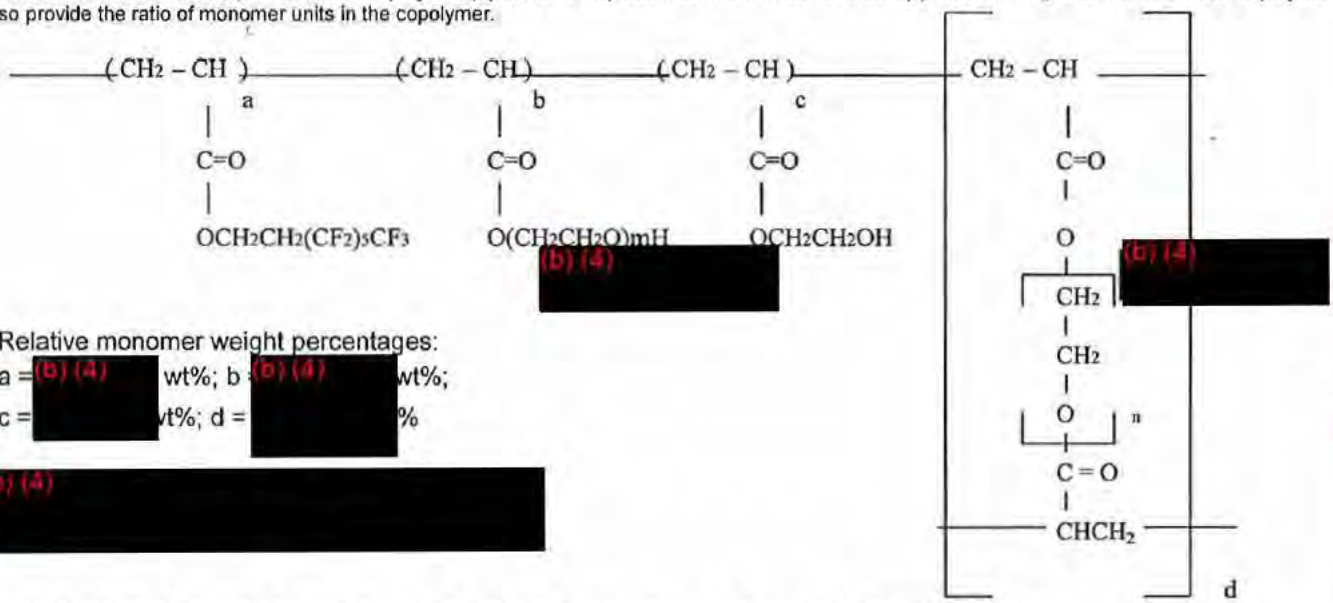
4. Other Chemical Names *(IUPAC, etc.)*

Perfluorohexylethyl acrylate-polyethylene glycol monoacrylate-2-hydroxyethyl acrylate-polyethylene glycol diacrylate copolymer

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



Relative monomer weight percentages:

a = (b) (4) [redacted] wt%; b = (b) (4) [redacted] wt%;

c = [redacted] wt%; d = [redacted] %

(b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

An IR spectrum of the FCS is available in **Attachment 2**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
Perfluorohexylethyl acrylate (13FA)	17527-29-6	Monomer	☒ Yes ☐ No
2-Hydroxyethyl acrylate (HEA)	818-61-1	Monomer	☒ Yes ☐ No
Polyethylene glycol monoacrylate (PEG monoacrylate)	26403-58-7	Monomer	☒ Yes ☐ No
Polyethylene glycol diacrylate (PEG diacrylate)	26570-48-9	Monomer	☒ Yes ■ No
(b) (4) [redacted]			
			☐ Yes ☐ No
* See **Attachment 3** for Certificates of Analysis for reagents.			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 4** for the CONFIDENTIAL manufacturing process diagram for the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
Perfluorohexylethyl acrylate (13FA)	17527-29-6	<50 ppm	CONFIDENTIAL	☒ Yes ☐ No
2-Hydroxyethyl acrylate (HEA)	818-61-1	<500 ppm		☒ Yes ☐ No
Polyethylene glycol monoacrylate (PEG monoacrylate)	26403-58-7	<50 ppm		☒ Yes ☐ No
Polyethylene glycol diacrylate (PEG diacrylate)	26570-48-9	<50 ppm		☒ Yes ☐ No
(b) (4)		<2000 ppm		☒ Yes ☐ No
		<50 ppm		☒ Yes ☐ No
		<20 ppm*		☒ Yes ☐ No
		60 ppb		☒ Yes ☐ No
		15 ppb		☒ Yes ☐ No
		248 ppm*		☒ Yes ☐ No
		<5000 ppm*		☒ Yes ☐ No
		<80 ppm*		☒ Yes ☐ No
		<100 ppm*		☒ Yes ☐ No

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* Data for these potential impurities are from testing on (b) (4) a copolymer that is structurally similar to (b) (4) and has a similar molecular weight.

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† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

For test results from residuals testing, see **Attachments 5, 6 and 7.**

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
Solids Content (%) [redacted]	(b) (4) [redacted]
pH (25°C) (b) (4)	
Specific Gravity (b) (4)	
Remaining solvent (%) (b) (4)	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Mw/Mn (See **Attachment 8**)			(b) (4) [redacted]
Tg (See **Attachment 9**)			

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

The percentage of the FCS with a MW <1000 daltons is approximately 0.033%. See **Attachment 8** for supporting SEC data.

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SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☒ Repeat Use

The polymer additive is intended to be used in paper and paperboard at a level not to exceed 0.4% dry weight. Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS may be applied at the size press or the wet end.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
As a polymer additive in paper and paperboard at a level not to exceed 0.4% dry weight.	All food types as described in Table 1 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html.	Conditions of Use A-H as described in Table 2 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

As stated above, the polymer additive is intended to be used in paper and paperboard at a level not to exceed 0.4% dry weight. Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS may be applied at the size press or the wet end.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 10 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 10 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

The FCS imparts grease and oil resistance to paper and paperboard. Test results demonstrating this technical effect can be found in **Attachment 10**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

No degradation of the FCS is anticipated during consumer use of paper or paperboard coated with the fluoropolymer. The results of thermogravimetric analysis on the FCS, which demonstrates its stability under proposed conditions of use, can be found in **Attachment 11**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
(b) (4)			

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Not applicable -- no migration testing was done for this FCS. See section II.F.2. of this form for a discussion of residual analyses that were done on the FCS. Exposure estimates were then conducted based on 100% migration of the residual level into food.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Not applicable.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable. See report of The National Food Laboratory for residual analyses in the dried polymer and validation of these analyses.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

A sample of the FCS was tested for residual monomers, oligomers, and for the presence of potential impurities. The CONFIDENTIAL composition of the test material can be found in **Attachment 12**.

The fluoropolymer was dissolved in acetone, and the resulting solution was analyzed by GC/MS for the monomers, (b)(4) were determined by a different laboratory using LC-MS. Residual amounts detected are provided in table II.B.3. of this form. Exposure estimates based on 100% migration of residuals are provided in **Attachment 13**. An example calculation, for 13FA follows:

Residual 13FA Monomer

1. The polymer is used at 0.4% in paper. (The product containing the polymer is used at 2.0%.)
2. The basis weight of paper is 0.050 g/in^2
3. Migration from paper to food is 100%
4. 10 g of food will contact each square inch of paper

The average residual level of 13FA monomer is <50 parts per million (ppm or μg/g). Assuming 100% of the 13FA will migrate to food:

$[(50\ \mu g_{13FA}/g_{polymer}) \times (0.05 g_{paper}/in^2) \times (0.2\ g_{polymer}/g_{solution}) \times (0.02\ g_{solution}/g_{paper})] \div 10 g_{food}/in^2 = 0.001\ \mu g_{13FA}/g_{food} \equiv 1.00$ ppb

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See **Attachment 13** for dietary concentration calculations for residual materials in the fluoropolymer FCS. As above, an example calculation, for 13FA follows:

Given a CF of 0.05 for specialty paper, the dietary concentration for 13FA is

1.00 ppb x 5% CF = 0.05 ppb, or 0.05 µg/kg

The EDI is 0.05 µg/kg x 3 kg/p/d = 0.15 µg/p/d

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 10 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 10 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Perfluorohexylethyl acrylate (13FA)	17527-29-6	1.0	0.05 ppb	0.15 µg/p/d	
2-Hydroxyethyl acrylate (HEA)	818-61-1	10.0	0.50 ppb	1.5 µg/p/d	
Polyethylene glycol monoacrylate (PEG monoacrylate)	26403-58-7	1.0	0.05 ppb	0.15 µg/p/d	
Polyethylene glycol diacrylate (PEG diacrylate)	26570-48-9	1.0	0.05 ppb	0.15 µg/p/d	
(b) (4) [redacted]		5.0	0.25 ppb	0.75 µg/p/d	
		100	5.0 ppb	1.5 µg/p/d	
		40.0	2.0 ppb	6.0 µg/p/d	
		1.0	0.05 ppb	0.15 µg/p/d	
		0.4	0.02 ppb	0.06 µg/p/d	
		1.2 ppt	0.06 ppt	0.18 ng/p/d	
		0.3 ppt	0.015 ppt	0.045 ng/p/d	
		1.6	0.08 ppb	0.24 µg/p/d	
		2.0	0.10 ppb	0.30 µg/p/d	
		6.6	0.33 ppb	0.99 µg/p/d	
		40 ppb	2.0 ppb	6.0 µg/p/d	

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: July 31, 2008

From: Division of Food Contact Notifications
Chemistry Team 2

Subject: FCN 827: Use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]poly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate as a grease-proofing agent for food-contact paper and paperboard.

To: Division of Food Contact Notifications
Regulatory Team 1
Attn: P. Honigfort, Ph.D

Daikin America submitted this food-contact notification (FCN 827) for the use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]poly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate as a grease-proofing agent for food-contact paper and paperboard. The food-contact substance (FCS) will be used at a level not to exceed 0.4% of the finished food-contact paper and paperboard.

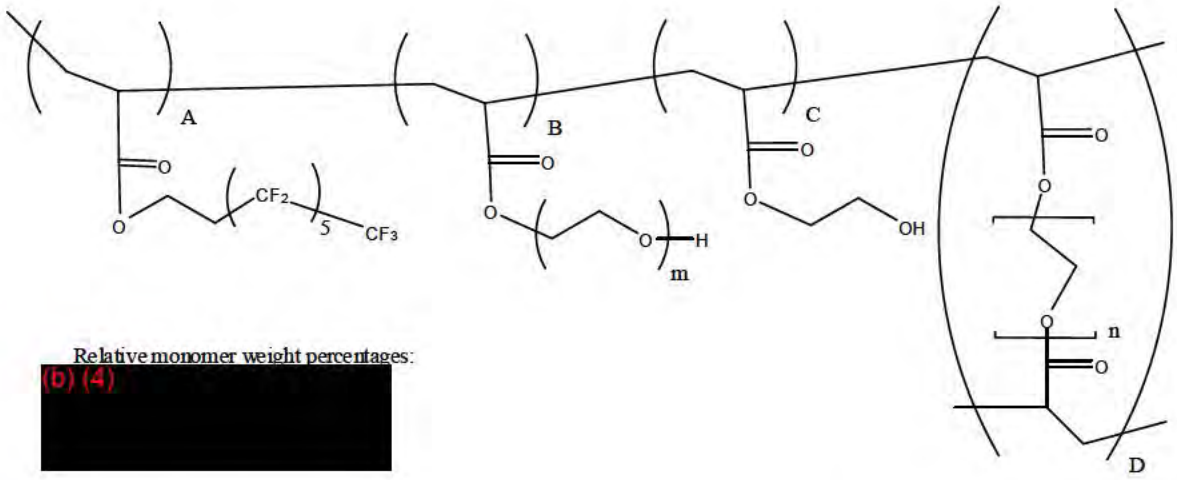
The FCS is not currently regulated or authorized for use in contact with food. There are numerous perfluoro-based grease-proofing agents regulated or authorized for use in contact with food. The FCSs identified in FCNs 628, 604, 599, 338, 311, and 206 are prepared from the same or similar perfluoroalkylethylacrylate monomers. FCN 820 was submitted by this notifier for the use of 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with alpha-(1-oxo-2-propen-1-yl)-omega-hydroxypoly(oxy-1,2-ethanediyl) as an oil and grease-proofing agent for food-contact paper and paperboard.

Identity

CAS Name:	2-Propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]poly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate
CAS Numbers:	1012783-70-8
Other Names:	Perfluorohexylethyl acrylate-polyethylene glycol monoacrylate-2-hydroxyethyl acrylate-polyethylene glycol diacrylate copolymer
Trade Name:	(b) (4) [redacted]

Molecular Weight: (b) (4) [redacted]

Structure:



Relative monomer weight percentages:
(b) (4) [redacted]

Spectroscopy

The notifier proved an IR spectrum in Attachment 2 of the FCN. The spectrum is consistent with the structure of the FCS. However, we note that this spectrum is identical to the spectrum submitted in FCN 820; therefore, IR spectroscopy cannot distinguish between these two materials. We requested in our deficiency letter dated 6/18/2008 that the notifier provide an unambiguous spectroscopic method of identifying this material. The notifier provided both proton and carbon-13 NMR spectra of the FCS described in this FCN and the FCS described in FCN 820. (b) (4) [redacted].

Manufacture

(b) (4) [redacted]

(b) (4) [redacted]

Intended Use/Use Level/Technical Effect

The FCS is intended to be used as a grease-proofing agent for food-contact paper and paperboard. The notifier provided data supporting the intended technical effect in Attachment 10 of the FCN. The FCS will be used at a level not to exceed 0.4% dry weight of the food-contact paper and paperboard. (b) (4) [redacted] the FCS will be applied only at the size press. The FCS will contact all food types under conditions of use A-H.

Stability

The notifier states that the FCS is stable under the intended conditions of use. The notifier provided a thermogravimetric analysis of the FCS in Attachment 11. The data support the notifier's conclusion that the material is stable under the requested use temperatures.

Migration Testing

Migration testing was not conducted in support of this notification. Instead, the notifier performed residue analyses for impurities in the finished FCS. The notifier performed gel-permeation chromatography (GPC) on the finished FCS to determine the residual level of oligomers in the FCS.

The notifier analyzed three lots of the FCS using gel-permeation chromatography/multiple-angle-laser-light-scattering (MALLS). The system was calibrated with polystyrene standards. The method was appropriately calibrated. Using this method, the notifier determined that there was approximately 1.7 weight-percent oligomers below 1600 Daltons.

For the FCS, Toxicology often requests that Chemistry calculate exposure to oligomers that have a molecular weight below 1000 Daltons. In reviewing the chemistry memoranda for various FCNs for perfluorinated grease-proofing agents, we note that we have provided Toxicology with exposure values variously based on 1000, 2200 and 2500 Daltons. In our memorandum on FCN 820 dated 7/2/2008 (K. Arvidson to M. Hepp) we devised, for our exposure estimates, a method for normalizing the molecular weight cutoff of perfluorinated oligomers with their hydrocarbon analogs. (b) (4) [redacted]

(b) (4) [redacted], 1600 Daltons.

In addition, there have been a number of discussions regarding the relative size of these perfluorinated oligomers versus their hydrocarbon analogs and how that might affect absorption in the gut. Although we cannot speak to the bioavailability of these perfluorinated species compared to their hydrocarbon analogs, we determined during our review of FCN 820 that there was little difference in the solvent-excluded volume1 of the perfluorinated polymer identified in that FCN and the hydrocarbon analog. Given that the relative ratio of perfluoro-based monomers and hydrocarbon based monomers in the FCS identified in this FCN and in the FCS identified FCN 820 are the same, we would expect little difference between the sizes of the oligomers.

The notifier analyzed triplicate samples of the FCS for residual perfluorohexylethyl acrylate, polyethylene glycol monoacrylate, 2-hydroxyethyl acrylate, and polyethylene glycol diacrylate (b) (4) [redacted] using gas chromatography/mass spectroscopy. The notifier prepared standard solutions of and calibration curves for each analyte. The correlation coefficients for each of the calibration curves are acceptable. Perfluorohexylethyl acrylate, polyethylene glycol monoacrylate, 2-hydroxyethyl acrylate, polyethylene glycol diacrylate, (b) (4) [redacted] were not detected in any of the replicate samples of the FCS above their respective limits of detection. These results were validated by spiking samples of the FCS with each of the analytes at their respective limits of detection. All spikes were detected.

The notifier did not analyzed the FCS for residual (b) (4) [redacted] Instead, the notifier wishes to rely on the residue levels for these materials reported in FCN 820. An evaluation of the manufacturing process has determined (b) (4) [redacted] used in the manufacture of both this FCS and the FCS identified in FCN 820. In both cases, the polymer solution is heated until all of the (b) (4) [redacted] has evaporated. Therefore, we can rely on the data submitted in FCN 820 for our exposure estimates. The residue level (b) (4) [redacted] would be less than 5000 µg/g FCS (the limit of detection, LOD). (b) (4) [redacted] As such, the residual level of (b) (4) [redacted] reported in FCN 820 (248 µg/g FCS) would represent a worst-case residue level of (b) (4) [redacted] in the manufacture of the FCS identified in this FCN. (b) [redacted] it is an impurity in perfluorohexylethylacrylate, (b) (4) [redacted]. Therefore, residue data from FCN 820 can be used to support exposure estimates for this FCN. The residual level of (b) (4) [redacted] reported in FCN 820 was less than 20 µg/g FCS (LOD). The analytical methods and data supporting the residue levels of (b) (4) [redacted] in Attachment 6 of this FCN and were evaluated and found acceptable in our review of FCN

1 . The solvent-excluded volume is the volume enclosed by the Connolly surface of a molecule. The Connolly surface is the surface, using a small spherical probe to simulate a solvent molecule, made by the center of the solvent sphere as it contacts the van der Waals surface of the molecule in question.

820.

(b) (4) [redacted]

Exposure Estimates

(b) (4) [redacted]

(b) (4) [redacted] We have evaluated and agree with the notifier's calculation.

Exposures were estimated using the residual levels of the respective impurities or the quantity of oligomers below 1600 Daltons (0.2%), the maximum requested application rate of the FCS at the size press (0.4% of dry paper), our standard assumption for the average basis weight of all food-contact paper and paperboard (0.05 g/in^2), our standard assumption for the quantity of food in contact with food packaging (10 g/in^2), the assumption of 100% migration to food, and a refined consumption factor of 0.01 (b) (4) [redacted] The dietary concentrations (DC) and estimated daily intake values are summarized in Table 1. A sample calculation using the oligomers is below.

$$DC = (0.01)\left(\frac{0.2\text{ g}}{100\text{ g FCS}}\right)\left(\frac{0.4\text{ g FCS}}{100\text{ g paper}}\right)\left(\frac{0.05\text{ g paper}}{1\text{ in}^2}\right)\left(\frac{1\text{ in}^2}{10\text{ g food}}\right)\left(\frac{1000\text{ g food}}{1\text{ kg food}}\right)\left(\frac{1000\text{ mg}}{1\text{ g}}\right)\left(\frac{1000\ \mu\text{g}}{1\text{ mg}}\right) = 0.4\ \mu\text{g/kg food (0.4 ppb)}$$

The estimated daily intake (EDI) is calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = (3\text{ kg food/p/d})(0.4\ \mu\text{g/kg food}) = 1.2\ \mu\text{g/p/d}$$

Cumulative Exposure Estimates

C6-based perfluoro oligomers

(b) (4) [redacted] In our chemistry memorandum dated 7/1/2008 on FCN 820 the cumulative DC and cumulative EDI were determined to be 1 ppb and 3 µg/p/d, respectively. (b) (4) [redacted] the DC for the C6 oligomers would increase by 0.4 ppb to 1.4 ppb. However, in all likelihood, this is an overestimate with the actual exposure somewhere between 1 and 1.4 ppb. The cumulative estimated daily intake would be 3-4.2 µg/p/d.

Impurities

Given the small EDIs for the impurities, they would not contribute to their respective CEDIs. Therefore, there will be no change in their cumulative EDIs.

Table 1. Exposure Estimates

	Residual level (µg/g FCS)	DC (ppb)	EDI (µg/p/d)
Oligomers (%)	0.2	0.4	1.2
13FA monomer	50	0.01	0.03
2-Hydroxyethyl acrylate	500	0.1	0.3
Polyethylene glycol monoacrylate	50	0.01	0.03
Polyethylene glycol diacrylate	50	0.01	0.03
(b) (4) [redacted]	248	0.05	0.2
	2000	0.4	1.2
	50	0.01	0.03
	20	0.004	0.01
	5000	1	3
	0.06	0.00001	0.00003
	0.015	0.000003	0.000009
		Regulated	21 CFR 176.170
		Regulated	21 CFR 176.170

Kirk Arvidson, Ph.D.

HFS-275 (R/F); HFS-705 (Diachenko)
HFS-275: KBArvidson:436-1152:FCN000820_C_MEMO:7/24/2008
R/D Init: MAAdams:7/29/2008
F/T:kba:7/30/2008

Impurities

Given the small EDIs for the impurities, they would not contribute to their respective CEDIs. Therefore, there will be no change in their cumulative EDIs.

Table 1. Exposure Estimates

	Residual level (µg/g FCS)	DC (ppb)	EDI (µg/p/d)
Oligomers (%)	0.2	0.4	1.2
13FA monomer	50	0.01	0.03
2-Hydroxyethyl acrylate	500	0.1	0.3
Polyethylene glycol monoacrylate	50	0.01	0.03
Polyethylene glycol diacrylate	50	0.01	0.03
(b) (4)	248	0.05	0.2
	2000	0.4	1.2
	50	0.01	0.03
	20	0.004	0.01
	5000	1	3
	0.06	0.00001	0.00003
	0.015	0.000003	0.000009
		Regulated	21 CFR 176.170
		Regulated	21 CFR 176.170

(b) (6)

Kirk Arvidson, Ph.D.

HFS-275 (R/F); HFS-705 (Diachenko)
HFS-275: KBArvidson:436-1152:FCN000820_C_MEMO:7/24/2008
R/D Init: MAAdams:7/29/2008
F/T:kba:7/30/2008

DAIKIN AMERICA FCN 888

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-hydroxyethyl ester, polymer with α-(1-oxo-2-propen-1-yl)-ω-hydroxypoly(oxy-1,2-ethanediyl), α-(1-oxo-2-propen-1-yl)-ω-[(1-oxo-2-propen-1-yl)oxy]poly(oxy-1,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate

2. CAS Registry Number

1012783-70-8

3. Trade or Common Name

(b) (4)

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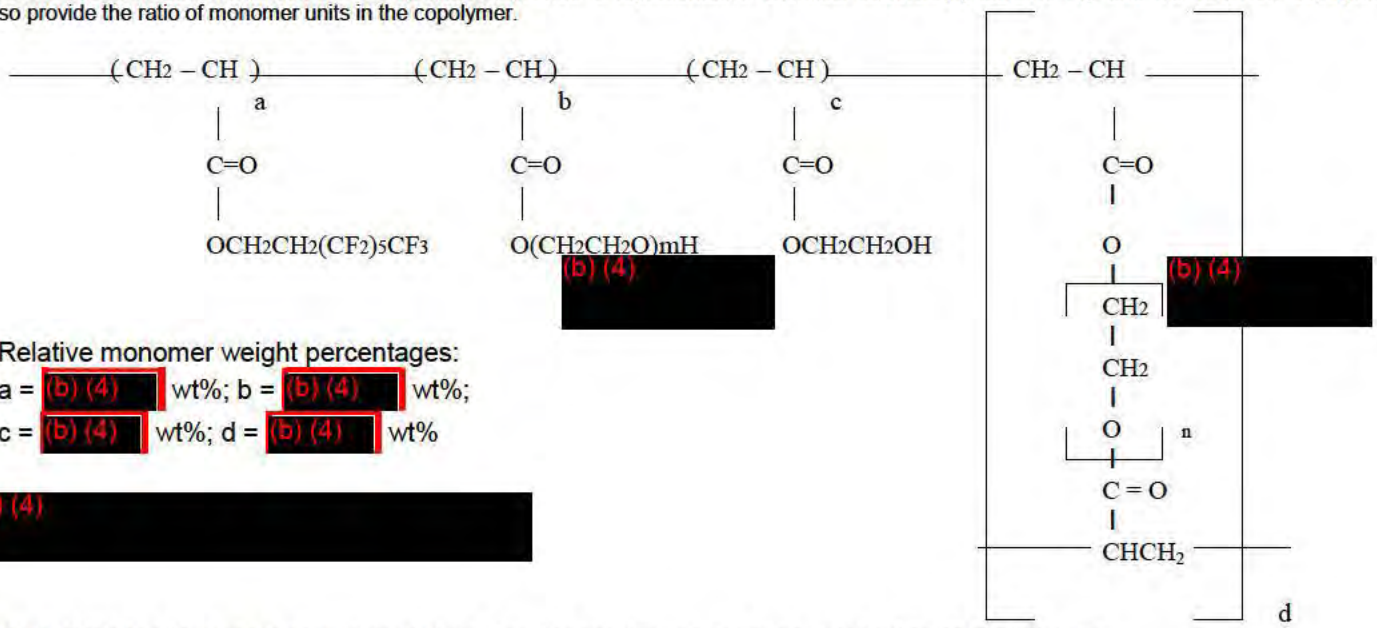
4. Other Chemical Names *(IUPAC, etc.)*

Perfluorohexylethyl acrylate-polyethylene glycol monoacrylate-2-hydroxyethyl acrylate-polyethylene glycol diacrylate copolymer

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



Relative monomer weight percentages:

a = (b) (4) wt%; b = (b) (4) wt%;

c = (b) (4) wt%; d = (b) (4) wt%

(b) (4)

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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See FCN 827

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
See FCN 827			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **FCN 827** for the CONFIDENTIAL manufacturing process diagram for the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
See FCN 827				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
See FCN 827	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Mw/Mn (See **Attachment 4**)	(b) (4)		
See FCN 827 for Tg			

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

See FCN 827, as amended. For convenience, the SEC data on the polymer as presently manufactured are also included as **Attachment 4**. These SEC data, which were also provided to FDA on January 6, 2009, to supplement FCN 827, show that percentage of the FCS with a MW <1000 daltons is less than 0.03%.

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SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☒ Repeat Use

The polymer additive is intended to be used at a level not to exceed 0.4% dry weight in paper and paperboard that will be used in food-contact applications with microwave susceptors.

Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS will be applied after sheet formation.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
As a polymer additive in paper and paperboard at a level not to exceed 0.4% dry weight	All food types as described in Table 1 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html.	Condition of Use J – microwave heat susceptor applications, as described in Table 2 of FDA's "Definitions of Food Types and Conditions of Use for Food Contact Substances," available at http://www.cfsan.fda.gov/~rdb/opa-fcn3.html

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

As stated above, the polymer additive is intended to be used at a level not to exceed 0.4% dry weight in paper and paperboard that will be used in food-contact applications with microwave susceptors. Treatment with the FCS will impart grease and oil resistance to the paper and paperboard. The FCS will be applied after sheet formation.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 5 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 5 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

See FCN 827.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

The FCS is stable at the temperatures that may be expected under microwave susceptor applications. The thermogravimetric analysis (TGA) curve submitted in FCN 827 shows that the polymer is stable at temperatures through 240°C.

Low levels of various volatiles were detected when film coated with (b) (4) was placed in a sealed headspace vial and heated for five minutes in a household microwave oven at the highest power setting, 750 watts. The headspace of the vial was then analyzed using gas chromatography-mass spectrometry (GC/MS) and an attempt was made to identify and quantify detected compounds by comparison with a standard library of mass spectrometry data (NIST). The concentrations in the headspace were determined using an internal standard, and were expressed as micrograms (µg) volatiles per square inch of extracted polymer. The very conservative assumption was then made that all the volatiles transferred to the food. The complete report by the National Food Laboratory is provided in **Attachment 2.**

Identities and structures of the 3 volatiles found at the highest concentrations are shown in Section II.E.2

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

(b) (4)

[redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Because the clearance provided in FCN 827 covers the use of the FCS in contact with all food under Conditions A through H, formal migration testing to cover the microwave susceptor applications was not performed. Rather, as noted in Section II. E.1., headspace analyses were performed by determining the potential volatile byproducts of the FCS that could evolve under microwave conditions. Volatiles were identified using a standard mass spectrometry library and quantified using an internal standard. They were then expressed as $\mu g/in^2$ of polymer. The full N.F.L. report is provided as Attachment 2.

For convenience of the reviewer, results of the headspace analysis are listed in Section F.1.c., below, even though they are not, strictly speaking, migration values.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
(b) (4)				0.3928, 0.0106, 0.0095 µg/in^2	**
				0.0476, 0.0017, 0.0026	
				0.0310, 0.0149, 0.0086	
				0.0942, 0.0253, 0.0366	
				0.3322, 0.0310, 0.0220	
				0.0887, 0.0399, 0.0589	
				1.3894, 0.3280, 0.4519	
				0.2212, 0.0198, 0.0126	
				0.0384, 0.0091, 0.0126	
				0.085, 0.0209, 0.0249	
				0.0872, 0.023, 0.0057	
				0.0217, 0.0064, 0.0057	
				0.1873, 0.0178, 0.0159	
				0.0996, 0.0197, 0.0212	
				0.0188, 0.0017, 0.002	
				0.0637, 0.0029, 0.0019	
				0.0643, 0.0027,0.0012	
				0.0842, 0.0027, 0.0021	

**** Averages not calculated, since significantly higher levels were found in the first sample. Risk assessment is based on the levels found in the first sample.**

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable. See report of The National Food Laboratory at **Attachment 2** for analyses of the volatile compounds released from the FCS under the intended conditions of use.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

The volatiles identified in the headspace analysis of the FCS after heating with a microwave oven were assumed to be completely absorbed by the food. Since one of the principal applications of microwave susceptor uses is in heating of pizza, we assumed that 5 grams of food is in contact with one square inch of polymer. Our assumptions are conservative, in that most of the volatiles are likely to remain in the headspace and not be absorbed by the food, which is removed from the microwave promptly after heating.

As an example, The National Food Laboratory determined that (b) (4) was present in headspace at a maximum level corresponding to 1.3894 $\mu g/in^2$ (3 samples). The concentration in food is therefore,

$1.3894\ \mu g/in^2 \div 5\ g_{food}/in^2 = 0.278\ \mu g/g_{food}$, or 278 parts per billion (ppb).

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

In II.F.2.(Migration Calculation Option), (b) (4) [redacted] concentration in food is estimated to be 278 ppb. FDA's consumption factor for microwave susceptor packaging is 0.001. Therefore, the dietary concentration, DC, is:

0.001 x 278 ppb = 0.278 ppb, or 0.278 µg/kg

The EDI is 0.278 µg/kg x 3 kg/p/d = 0.834 µg/p/d, or 0.834 x 10^{-3} mg/p/d

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

While we are not aware of any repeated use applications for the FCS, we include them as an option here so as to not preclude the use of the FCS in repeated-use applications. In estimating exposure to the FCS and its potential impurities in this FCN, we have assumed 5 grams of food will contact each square inch of the FCS. In a repeated-use application, the amount of food contacting one square inch of FCS would be greater than 5 grams, so the exposures estimated in this FCN can be considered worst-case, and will cover both single-use and repeated-use applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
(b) (4)		79	0.079	0.234×10^{-3}	
		9.52	0.01	0.0285×10^{-3}	
		6.20	0.006	0.0186×10^{-3}	
		18.8	0.02	0.0564×10^{-3}	
		66.4	0.07	0.199×10^{-3}	
		17.7	0.02	0.053×10^{-3}	
		277.9	0.278	0.834×10^{-3}	0.33
		44.2	0.04	0.132×10^{-3}	
		7.68	0.008	0.231×10^{-3}	
		17.0	0.017	0.051×10^{-3}	
		17.4	0.017	0.051×10^{-3}	
		4.34	0.004	0.012×10^{-3}	
		37.5	0.04	0.114×10^{-3}	
		19.9	0.02	0.06×10^{-3}	
		3.76	0.004	0.012×10^{-3}	
		12.7	0.01	0.0381×10^{-3}	
		12.9	0.01	0.0387×10^{-3}	
		16.5	0.02	0.0504×10^{-3}	

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: November 30, 2009

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 888:** Keller and Heckman LLP (K&H) on behalf of Daikin America (Daikin). Use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]poly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate. Submission received February 18, 2009.

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 1
Attention: P. Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of Daikin America (Daikin), submitted this food contact notification (FCN) to allow for the use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]poly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate (CAS Reg. No. 1012783-70-8) as an oil and grease resistant treatment for paper and paperboard employed at the size press. The food contact substance (FCS) may be used at a level not to exceed 0.4 % by weight of dry paper and paperboard intended for use in contact with all food types under Condition of Use J (microwave susceptor applications only).

The May 27, 2009 Memorandum to the File for FCN 888 (P. Honigfort) provided exposure estimates to the C6 based low molecular weight oligomers (LMWOs) and to non-volatile migrants in the FCS based on the following assumptions:

1) For LMWOs: the gel permeation chromatography data provided in Attachment 4 of FCN 888 indicated that the maximum level of LMWOs (<1600 D) is <0.04 wt.-%; for non-volatile migrants: residual levels were provided in Section II.B of FCN 827,
2) the proposed use level of the FCS at the size press (0.4% of dry paper),
3) an average basis weight of 0.05 g/in^2 for all food-contact paper and paperboard,
4) the assumption that 5 g food contacts 1 in^2 microwave susceptor packaging,
5) the assumption of 100% migration to food, and
6) a CF of 0.001.

The average basis weight for all food-contact paper and paperboard used for use condition J should be 0.023 g/in^2 (rather than 0.05 g/in^2). Exposure to all migrants using the corrected basis weight is provided in Table 1 below. We note that these exposures are lower than the exposures calculated in the May 27, 2009 memorandum to the file. A sample calculation for LMWOs is shown below.

$$DC_{LMWO} = \frac{(0.0004 \text{ g LMWO/g FCS})(0.004 \text{ g FCS/g paper})(0.023 \text{ g paper/in}^2 \text{ paper})(0.001)}{(5 \text{ g food/in}^2 \text{ paper})}$$

Memorandum

Date: November 30, 2009

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 888:** Keller and Heckman LLP (K&H) on behalf of Daikin America (Daikin). Use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(1-oxo-2-propen-1-yl)-ω-hydroxypoly(oxy-1,2-ethanediyl), α-(1-oxo-2-propen-1-yl)-ω-[(1-oxo-2-propen-1-yl)oxy]poly(oxy-1,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate. Submission received February 18, 2009.

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 1
Attention: P. Honigfort, Ph.D.

Keller and Heckman LLP (K&H), on behalf of Daikin America (Daikin), submitted this food contact notification (FCN) to allow for the use of 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(1-oxo-2-propen-1-yl)-ω-hydroxypoly(oxy-1,2-ethanediyl), α-(1-oxo-2-propen-1-yl)-ω-[(1-oxo-2-propen-1-yl)oxy]poly(oxy-1,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate (CAS Reg. No. 1012783-70-8) as an oil and grease resistant treatment for paper and paperboard employed at the size press. The food contact substance (FCS) may be used at a level not to exceed 0.4 % by weight of dry paper and paperboard intended for use in contact with all food types under Condition of Use J (microwave susceptor applications only).

The May 27, 2009 Memorandum to the File for FCN 888 (P. Honigfort) provided exposure estimates to the C6 based low molecular weight oligomers (LMWOs) and to non-volatile migrants in the FCS based on the following assumptions:

1) For LMWOs: the gel permeation chromatography data provided in Attachment 4 of FCN 888 indicated that the maximum level of LMWOs (<1600 D) is <0.04 wt.-%; for non-volatile migrants: residual levels were provided in Section II.B of FCN 827,
2) the proposed use level of the FCS at the size press (0.4% of dry paper),
3) an average basis weight of 0.05 g/in^2 for all food-contact paper and paperboard,
4) the assumption that 5 g food contacts 1 in^2 microwave susceptor packaging,
5) the assumption of 100% migration to food, and
6) a CF of 0.001.

The average basis weight for all food-contact paper and paperboard used for use condition J should be 0.023 g/in^2 (rather than 0.05 g/in^2). Exposure to all migrants using the corrected basis weight is provided in Table 1 below. We note that these exposures are lower than the exposures calculated in the May 27, 2009 memorandum to the file. A sample calculation for LMWOs is shown below.

$$DC_{LMWO} = \frac{(0.0004 \text{ g LMWO/g FCS})(0.004 \text{ g FCS/g paper})(0.023 \text{ g paper/in}^2 \text{ paper})(0.001)}{(5 \text{ g food/in}^2 \text{ paper})}$$

= $7.4x10^{-12}$ g LMWOs/g food = 7.4 pptr

Table 1: Exposure Estimates to LMWOs and Non-Volatile Migrants

Migrant	CAS No.	Max residual level (µg/g FCS)*	DC (pptr)
LMWOs		0.04%	7.4
Perfluorohexylethyl acrylate	17527-29-6	50	0.9
2-Hydroxyethyl acrylate	818-61-1	500	9
Polyethylene glycol monoacrylate	26403-58-7	50	0.9
Polyethylene glycol diacrylate)	26570-48-9	50	0.9
(b) (4) [redacted]		248	4.6
		2000	37
		50	0.9
		20	0.4
		5000	92
		0.06	1 ppqd
		0.015	0.3 ppqd
		Regulated	§176.170
		Regulated	§176.170

* For LMWOs, the gel permeation chromatography data provided in Attachment 4 of FCN 888 indicated that the maximum level of LMWOs (<1600 D) is <0.04 wt.-%. For non-volatile migrants, residual levels were provided in Part II, Section B of FDA Form 3480 of FCN 827.

As indicated in the May 27, 2009 memorandum to the file, the DC of 7.4 pptr for the C6 based LMWO fraction resulting from the use of the FCS as per FCN 888 would be subsumed by the cumulative DC for C6 oligomers. In addition, given the small DC for the non-volatile impurities, they would not contribute to their respective CDCs. Therefore, there will be no change in their CDCs.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb: FCN888C_memo
RDInit: ABBailey, 11-30-09
Final: seb, 11-30-09

$= 7.4x10^{-12}$ g LMWOs/g food = 7.4 pptr

Table 1: Exposure Estimates to LMWOs and Non-Volatile Migrants

Migrant	CAS No.	Max residual level (μg/g FCS)*	DC (pptr)
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2-Hydroxyethyl acrylate	818-61-1	500	9
Polyethylene glycol monoacrylate	26403-58-7	50	0.9
Polyethylene glycol diacrylate)	26570-48-9	50	0.9
(b) (6) [redacted]		248	4.6
		2000	37
		50	0.9
		20	0.4
		5000	92
		0.06	1 ppqd
		0.015	0.3 ppqd
		Regulated	§176.170
		Regulated	§176.170

* For LMWOs, the gel permeation chromatography data provided in Attachment 4 of FCN 888 indicated that the maximum level of LMWOs (<1600 D) is <0.04 wt.-%. For non-volatile migrants, residual levels were provided in Part II, Section B of FDA Form 3480 of FCN 827.

As indicated in the May 27, 2009 memorandum to the file, the DC of 7.4 pptr for the C6 based LMWO fraction resulting from the use of the FCS as per FCN 888 would be subsumed by the cumulative DC for C6 oligomers. In addition, given the small DC for the non-volatile impurities, they would not contribute to their respective CDCs. Therefore, there will be no change in their CDCs.

Conclusion

We have no questions on this FCN.

(b) (6) [redacted]

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb: FCN888C_memo
RDInit: ABBailey, 11-30-09
Final: seb, 11-30-09

AD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: February 12, 2009

From: Division of Food Contact Notifications (HFS-275)
Chemistry Review Team I
Karen R. Hatwell, Ph.D.

Subject: (b) (4) : Keller & Heckman (K&H) on behalf of Daikin America. (b) (4)
Submission received January 12, 2009 and additional information received February 5, 2009 (email).

To: Division of Food Contact Notifications
Paul Honigfort, Ph.D.

(b) (4)

K&H provided additional information that includes updated molecular weight data (document titled "Additional Information" contained in the January 12, 2009 submission) and updated manufacturing process information (document titled "Information on process change" contained in the February 5, 2009 submission).

First we will present a summary of the chemistry information on FCN 827 (b) (4)

Background

FCN 827 notified the use of the food contact substance (FCS) identified as 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(1-oxo-2-propen-1-yl)-ω-hydroxypoly(oxy-1,2-ethanediyl), α-1-oxo-2-propen-1-yl)-ω-[(1-oxo-2-propen-1-yl)oxy]poly(oxy-1,2-ethanedyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate (CAS Reg. No. 1012783-70-8, (b) (4) at levels up to 0.4% (dry weight) in the manufacture of food-contact paper and paperboard that will contact all food types under Conditions of Use A-H[1].

(b) (4)

[1] Chemistry memorandum on FCN 827 dated 7/31/08 (K. Arvidson to P. Honigfort).

fraction would not exceed 0.5 ppb. As discussed in the 7/31/08 chemistry memorandum, the LMWO fraction of <1600 D was 0.2 wt.-%. We calculated exposure assuming the following:

1. the maximum level of LMWO (<1600 D) was 0.2 wt.-%,
2. requested application rate of the FCS at the size press (0.4% of dry paper),
3. our standard assumption for the average basis weight of all food-contact paper and paperboard (0.05 g/in^2),
4. our standard assumption for the quantity of food in contact with food packaging (10 g/in^2),
5. the assumption of 100% migration to food, and

(b) (4) [redacted]

The DC of the FCS (expressed as LMWO) was calculated to be 0.4 ppb:

$$DC = (0.01)\left(\frac{0.2\text{ g}}{100\text{ g FCS}}\right)\left(\frac{0.4\text{ g FCS}}{100\text{ g paper}}\right)\left(\frac{0.05\text{ g paper}}{1\text{ in}^2}\right)\left(\frac{1\text{ in}^2}{10\text{ g food}}\right)\left(\frac{1000\text{ g food}}{1\text{ kg food}}\right)\left(\frac{1000\text{ mg}}{1\text{ g}}\right)\left(\frac{1000\ \mu\text{g}}{1\text{ mg}}\right) = 0.4\ \mu\text{g/kg food (0.4 ppb)}$$

The estimated daily intake (EDI) was calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = (3\text{ kg food/p/d})(0.4\ \mu\text{g/kg food}) = 1.2\ \mu\text{g/p/d}$$

Comments

K&H state that no changes have been made in the manufacturing process. However, optimization of manufacturing practices, detailed in "Additional information," have resulted in a product will consistently lower LMWOs.

Analysis of the several batches of the FCS was performed by Sumika Chemical Analysis Service, Ltd. (analytical report dated 11/14/08) using gel permeation chromatography coupled with multiangle laser light scattering photometer (GPC-LC). A 0.5 g portion of the test substance was dissolved in tetrahydrofuran (THF, 10 mL). The samples were compared to polystyrene standards. Six samples of the FCS were tested in duplicate. The results are shown in Table 2 (as taken from Section 4 of the report, p. 2/15).

Table 1. Batch molecular weight analysis of (b) (4) [redacted]

Sample	No. of tests	Mn	Mw	Mw/Mn	Ratio of MW <2500
(b) (4) [redacted]					

[redacted]

The results generally confirm the notifier's claim that optimization of the manufacturing process has led to LMWO levels <0.04 (<1600 Dalton). The data is acceptable.

The notifier requests that the average fraction of the LMWO (<1600 D) be changed to less than 0.04% and that the entire CF for grease resistant paper (5%) be used along with the previous assumptions in FCN 827. This would change the calculation.

$$DC = (0.05)\left(\frac{0.4\text{ g}}{100\text{ g FCS}}\right)\left(\frac{0.04\text{ g FCS}}{100\text{ g paper}}\right)\left(\frac{0.05\text{ g paper}}{1\text{ in}^2}\right)\left(\frac{1\text{ in}^2}{10\text{ g food}}\right)\left(\frac{1000\text{ g food}}{1\text{ kg food}}\right)\left(\frac{1000\text{ mg}}{1\text{ g}}\right)\left(\frac{1000\ \mu\text{g}}{1\text{ mg}}\right) = 0.4\ \mu\text{g/kg food (0.4 ppb)}$$

(b) (4) [redacted]

Summary

(b) (4) [redacted]

(b) (6) [redacted]

Karen R. Hatwell, Ph.D.

HFS-275 (R/F); HFS-705 (Diachenko)
HFS-275:KHatwell:436-1171: KH:02/09/09 (b) (4) [redacted])
Init:ABailey: 02/12/09
Final:KH: 02/12/09

From: Elyashiv-Barad, Sharon
Sent: Thursday, June 11, 2009 12:25 PM
To: Honigfort, Paul
Cc: Hatwell, Karen; Bailey, Allan B
Subject: Cumulative exposure to C6 LMWOs (related to FCNs 888, 827 and (b) (4)

Hi Paul,

I spoke to Allan this morning about the cumulative exposure to C6 oligomers. I pointed out that the February 12, 2009 chemistry memorandum for (b) (4) That chemistry memorandum only discussed the dietary concentration for the LMWOs, not the cumulative exposure. The cumulative exposure was addressed however, in Section IV, Item c (Exposure to the C6 based LMWO fraction of the FCS) of the May 27, 2009 summary memorandum for FCN 888. As indicated in the summary memorandum, "The DC of 16 pptr for the C6 based LMWO fraction resulting from the use of the FCS per FCN 888 would be subsumed by the cumulative DC of 1 ppb for C6 oligomers". A discussion of how the cumulative was calculated is also provided in that section. The summary memo also included a discussion of the regulatory status/background of the FCS (b) (4) (See Section II of the memo).

As such, there is no need for an additional memorandum to address the cumulative exposure to C6 oligomers.

-Sharon

Sharon Elyashiv-Barad, Ph.D.
Regulatory Review Chemist
Division of Food Contact Notifications
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration

5100 Paint Branch Pkwy; HFS-275
College Park, MD 20740

Tel: (301)436-1169 Fax: (301)436-2965

DAIKIN AMERICA FCN 933

FORM 3480 WAS MISSING
FROM THE FOIA RESPONSE

Memorandum

Date: December 1, 2009

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 933:** Keller and Heckman on behalf of Daikin America (Daikin). Use of 2-propenoic acid, 2-methyl-, polymer with 2-hydroxyethyl 2-methyl-2-propenoate, α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate, sodium salt as a grease-proofing agent in food-contact paper and paperboard. Submission received September 1, 2009.

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 1
Attention: K. Randolph, D.V.M., M.P.H.

Keller and Heckman on behalf of Daikin America (Daikin) submitted this food contact notification (FCN) for use of 2-propenoic acid, 2-methyl-, polymer with 2-hydroxyethyl 2-methyl-2-propenoate, α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate, sodium salt as a grease-proofing agent for food-contact paper and paperboard employed at the size press or wet-end in contact with all foods under Conditions of Use A through H and J (including microwave susceptor applications). The food-contact substance (FCS) will be used at a level not to exceed 0.8 weight-percent (wt.-%) of the finished food-contact paper and paperboard. (b) (4)
(b) (4)

Background

The FCS is not currently regulated under 21 CFR 170-199 nor is it the subject of any effective FCNs. There are numerous perfluoro-based grease-proofing agents regulated or authorized for use in contact with food. The FCSs identified in Daikin's FCNs 820[1] (effective July 31, 2008), 827[2] (effective September 9, 2008) and 888[3] (effective June 18, 2009) are prepared from the same or similar perfluoroalkylethylacrylate monomers:

1. FCN 820- 2-propenoic acid, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl ester, polymer with α-(1-oxo-2-propen-1-yl)- ω -hydroxypoly(oxy-1,2-ethanediyl) as an oil and grease-proofing agent for food-contact paper and paperboard employed at the size press at levels not to exceed (NTE) 0.2 wt.-% of the finished food-contact paper.
2. FCN 827- 2-propenoic acid, 2-hydroxyethyl ester, polymer with α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl), α-(1-oxo-2-propen-l-yl)-ω-[(l-oxo-2-propen-l-yl)oxy]-poly

[1] Chemistry memorandum for FCN 820 dated July 1, 2008 (K. Arvidson to M. Hepp).
[2] Chemistry memorandum for FCN 827 dated July 31, 2008 (K. Arvidson to P. Honigfort).
[3] Memorandum to the File for FCN 888 dated May 27, 2009 (P. Honigfort).

(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate as a grease-proofing agent for food-contact paper and paperboard employed at the size press, at levels NTE 0.4 wt.-%, under Conditions of Use A through H.

3. FCN 888- expanded FCN 827 to include use in microwave susceptor applications (Condition of Use J).

FCNs 820 and 827 were initially submitted for use of the FCS in food-contact paper and paperboard employed at the size press or wet-end. (b) (4) (b) (4)

Chemistry information is contained in FDA Form 3480 and Attachments 2 (IR spectrum), 3 (certificates of analysis for reagents), 4 (manufacturing diagram), 5 (test results for potential impurities in the FCS), 6 (test results for residual (b) (4), 7 (test results for residual (b) (4) 8 (test results for residual (b) (4) (b) (4), 9 (analysis of volatile compounds released from fluoropolymer heated in a microwave oven), 10 (molecular weight distribution. MWD, data), 11 (technical data sheet), 12 (thermogravimetric analysis, TGA, of the FCS), 13 (exposure calculations). The suggested language for the FCN is provided in Attachment 21.

Identity

Information on the identity of the FCS is contained in Form 3480, Sections II.A and II.C, and Attachments 2, 3 and 10.

(b) (4)

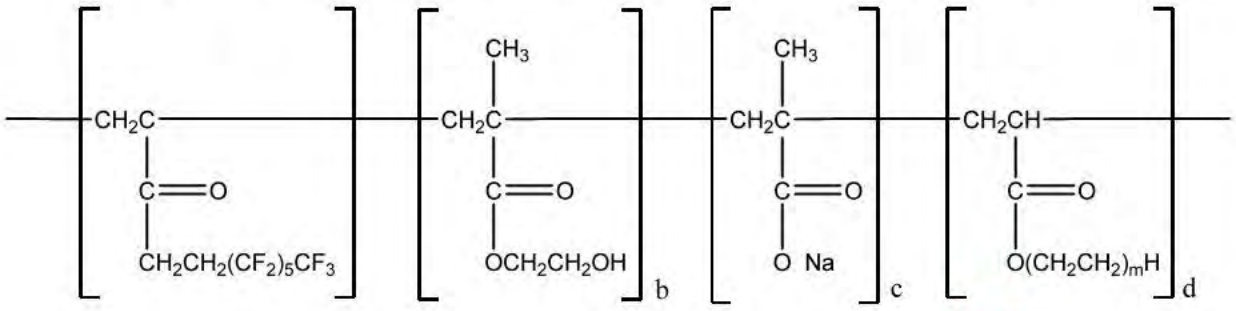
CAS name:	2-propenoic acid, 2-methyl-, polymer with 2-hydroxyethyl 2-methyl-2-propenoate, α-(l-oxo-2-propen-l-yl)-ω-hydroxypoly(oxy-l,2-ethanediyl) and 3,3,4,4,5,5,6,6,7,7,8,8,8 -tridecafluorooctyl 2-propenoate, sodium salt
CAS Reg. No.:	1158951-86-0
Other names:	Copolymer of C-6 fluoroacrylate, 2-hydroxyethyl methacrylate, polyethylene glycol monoacrylate and methacrylic acid
Trade names:	(b) (4)
Structure:	The structure of the FCS, as taken from Section II.A.5, is shown below.

P fluo oh xyl thyl c yl t (13F)

2-Hyd oxy thyl th c yl t (HEM)

M th c ylic cid (MM)

Poly thyl n lycol ono c yl t (PEGM)



(b) (4)

Monomer mole ratios:

(b) (4)

FCS specifications: In Section II.C, the notifier provided specifications for the FCS (solids content, pH, specific gravity and % solvent in the FCS). Attachment 3 contains the method used for determining the amount of solvent in the product.

FCS Analysis: Attachment 2 contains an IR spectrum that supports the structure of the FCS.

Molecular weight distribution (MWD)

Attachment 10 contains gel permeation chromatography (GPC) data for four batches (dry) of the commercial product.

(b) (4)

We would like to note that for the FCS, Toxicology typically requests that we calculate exposure to the fraction of oligomers <1000 Daltons. In reviewing the chemistry memoranda for various FCNs for other perfluorinated grease-proofing agents we have previously provided toxicology with exposure values based on the MW fractions with <1000, 2200 and 2500 D. In addition, there have been a number of discussions regarding the relative size of these perfluorinated oligomers versus their hydrocarbon analogs and how that might affect absorption in the gut. While chemistry cannot speak to the bioavailability of these perfluorinated species compared to their hydrocarbon analogs, we can provide some insight into their relative size. Using Chem3D Ultra5 version 6.0, we have determined the solvent-excluded volume and MW of a representative repeat unit in the FCS and the analogous hydrocarbon version of that same repeat unit.

(b) (4)

(b) (4)

(b) (4)

We have no questions on the identity of the FCS.

Manufacture

(b) (4)

[4] Chemistry memorandum for FCN 885 dated May 14, 2009 (S. Elyashiv-Barad to P. Honigfort). FCN 885 was submitted by DuPont Chemical Solutions Enterprise for use of a perfluoroalkylethyl methacrylate copolymer as an oil and grease resistant treatment for paper and paperboard intended for use under Conditions of Use B through H and J (microwave susceptor applications).

Table 1: Materials used to manufacture the FCS

Reagants	CAS Reg. #	Function	Amount used (kg)
Perfluorohexylethyl acrylate (13FA)	17527-29-6	Monomer	(b) (4)
2-Hydroxyethyl methacrylate (HEMA)	868-77-9	Monomer	(b) (4)
Polyethylene glycol monoacrylate (PEGMA or AE200)	26403-58-7	Monomer	(b) (4)
Methacrylic acid (MMA)	79-41-4	Monomer	(b) (4)
(b) (4)			

(b) (4)

Impurities

(b) (4)

Attachment 5: Determination of residual polymerization aids, solvents and impurities in the "dry" commercial product by GC-MS

(b) (4)

(b) (4)

(b) (4)

(b) (4)

The typical residual levels of impurities in the FCS on a dry basis, as taken from Section II.B.3, are summarized in Table 2, below.

Table 2: Summary of impurities in the "dry" commercial product

(b) (4)

We have no questions on the manufacture of the FCS or impurities in the FCS.

Intended Use and Technical Effect

Information on the intended use and technical effect of the FCS is contained in Form 3480, Section

II.D., and Attachment 11

The FCS is intended to be used as a grease-proofing agent for food-contact paper and paperboard employed either prior to the sheet forming operation (aka wet-end) or at the size press. The FCS is used at a level not to exceed 0.8 wt.-% dry weight of the food-contact paper and paperboard (b) (4) (b) (4) The FCS may contact all foods under Conditions of Use A through H and J (microwave heat-susceptor packaging).

The notifier provided a technical data sheet for the commercial product in Attachment 11. The suggested language for the FCS is contained in Attachment 21. We concur with this language.

We have no questions on the intended use and technical effect of the FCS.

Stability

Information on the stability of the FCS is contained in Sections II.E, II.F, and Attachments 9 and 12. The notifier states that the FCS is stable under the proposed use and notes that the thermogravimetric analysis (TGA) curve submitted in Attachment 12 supports the stability of the FCS.

(b) (4)

(b) (4)

(b) (4)

We have no questions on the stability of the FCS under the proposed conditions of use.

Consumer Exposure

The notifier did not carry out migration studies to support of the proposed use. Rather, in Form 3480, Section II.F.2, the notifier calculated migration of FCS oligomers and impurities separately for Conditions of Use A through H and J based on the assumption of 100% migration to food, the residual levels of impurities (from Section II.B.3), volatiles (from Section F.1.c) or the quantity of oligomers (b) (4) combined with the maximum requested application rate of the FCS at the size press (0.8 wt.-% of dry paper).

For Conditions of Use A through H, the notifier used FDA's standard assumption for the average basis weight of all food-contact paper and paperboard (0.05 g paper/in^2), the assumption that 10 g of food contacts 1 in^2 of food packaging, and a consumption factor (CF) of 0.05 for specialty paper. For Condition of Use J, the notifier used FDA's standard assumption for the average basis weight of all food-contact paper and paperboard (0.023 g paper/in^2), the assumption that 5 g of food contacts 1 in^2 of microwave susceptor packaging, and the CF for microwave susceptor packaging (0.001). Exposure estimates were provided in Attachment 13, and are summarized in Tables 4 and 5, below. We note that the notifier did not estimate exposure to non-volatile migrants under Conditions of Use J. As can be seen in Table 4, exposures from Condition of Use J were negligible in comparison. As such, we concur with the notifier's approach and exposure estimates.

A sample exposure calculation for LMWOs is provided below.

LMWOs: Condition of Use A-H

$$< M >_{Oligomers,\,A-H} = \frac{0.004\,g\,LMWO}{100\,g\,FCS}\,x\,\frac{0.8\,g\,FCS}{100\,g\,paper}\,x\,\frac{0.05\,g\,paper}{in^2}\,x\,\frac{in^2}{10\,g\,food} = 1.6\,\mu g\,LMWO/kg\,food$$

$$DC_{Oligomers,\,A-H} = 0.05\,x\,1.6\,\mu g\,LMWO/kg\,food = 0.08\,\mu g\,LMWO/kg\,food = 0.08\,ppb$$

LMWOs: Condition of Use J

$$< M >_{Oligomers,\,J} = \frac{0.004\,g\,LMWO}{100\,g\,FCS}\,x\,\frac{0.8\,g\,FCS}{100\,g\,paper}\,x\,\frac{0.023\,g\,paper}{in^2}\,x\,\frac{in^2}{5\,g\,food} = 1.5\,\mu g\,LMWO/kg\,food$$

$$DC_{Oligomers,\,J} = 0.001\,x\,1.5\,\mu g\,LMWO/kg\,food = 1.5\,ng\,LMWO/kg\,food = 1.5\,pptr$$

LMWOs: Total exposure

$$DC_{Oligomers,total} = DC_{Oligomers,\,A-H} + DC_{Oligomers,\,J} = 0.8\,ppb + 1.5\,pptr = 0.8\,ppb$$

Table 4: Exposure estimates to non-volatile migrants (Conditions of Use A-H and J)

(b) (4)

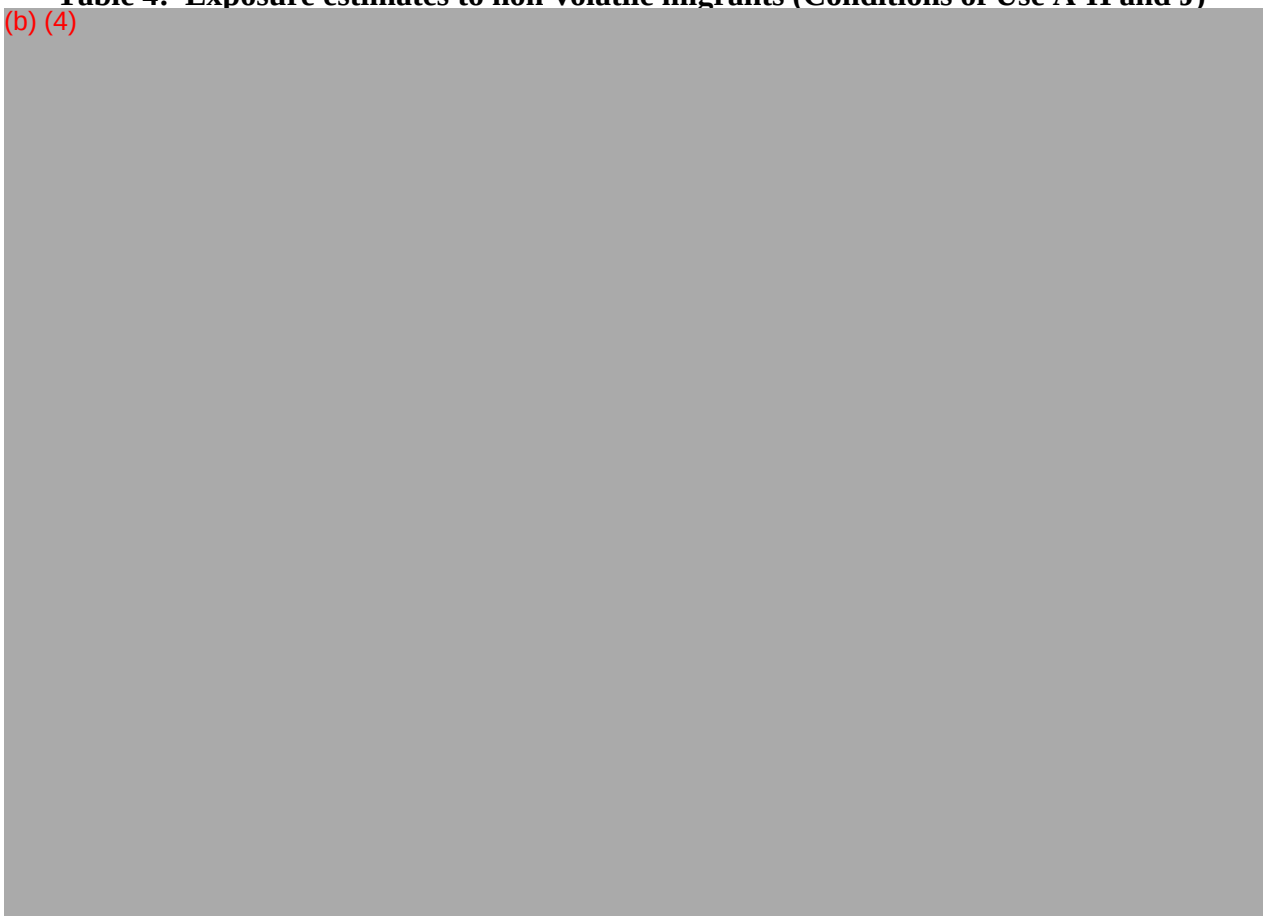


Table 5: Exposure estimates to volatile migrants

(b) (4)

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We have no questions on consumer exposure.

Notification Language

The acknowledgment letter, signed off by Chemistry on September 30, 2009, is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

(b) (5)

Table 5: Exposure estimates to volatile migrants

(b) (4)

[redacted]

(b) (4)

[redacted]

We have no questions on consumer exposure.

Notification Language

The acknowledgment letter, signed off by Chemistry on September 30, 2009, is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

(b) (5)

[redacted]

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Attachment 2

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Attachment 3

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Attachment 5

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Attachment 6

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Attachment 7

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Attachment 8

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Attachment 9

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Attachment 11

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Attachment 10

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Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propenoic acid, 2-methyl-, 2-hydroxyethyl ester, polymer with 1-ethenyl-2-pyrrolidinone, 2-propenoic acid and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl 2-propenoate, sodium salt

2. CAS Registry Number

1206450-10-3

3. Trade or Common Name

(b) (4)

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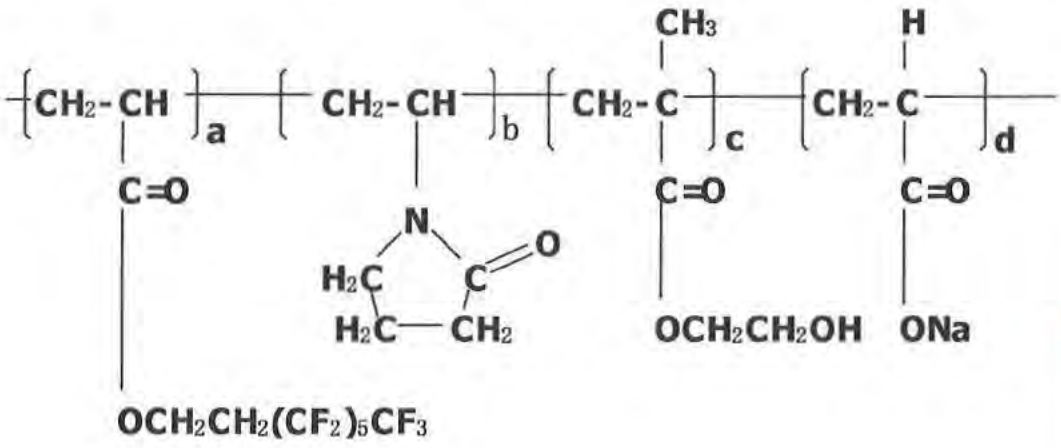
4. Other Chemical Names *(IUPAC, etc.)*

Copolymer of C-6 fluoroacrylate, 1-vinyl-2-pyrrolidone, 2-hydroxyethyl methacrylate, and acrylic acid

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.



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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
(b) (4) [redacted]			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

(b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
(b) (4)				

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
(b) (4)	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
Mw/Mn (*See* **Attachment 3:** GPC-MALLS (b) (4))			(b) (4)
Glass transition points (*See* **Attachment 14** of (b) (4))			(b) (4)

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

We note that FDA generally considers the fraction of the polymer having a molecular weight of less than 1,000 daltons to be the fraction that is capable of migrating to food and being absorbed in the body (and thus having the potential to be toxicologically significant) if ingested. As such, we generally consider only this fraction when determining the potential dietary exposure to a polymer. However, because migration and absorption are thought to be primarily a function of molecular size, rather than strictly molecular weight, it is expected that perfluorooligomer may be more absorbed for a given molecular weight than oligomers of a polymer composed only of carbon, hydrogen, and oxygen. In the case of this fluoroacrylate copolymer, the ratio of non-13FA monomer units to 13FA units is (b) (4) Therefore, the molecular weight above which oligomer absorption is not likely can be estimated by molar proportion:

(b) (4)

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Specifically, examination of the GPC curves from three analyses demonstrate that no more than (b) (4) of the polymer has molecular weight of 2000 daltons and below. As shown above, this fraction will include all relevant low molecular weight oligomers.

See **Attachments 1, 2, and 3** for the GPC data.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☐ Single Use ☐ Repeat Use

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
(b) (4)		

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

(b) (4)

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
(b) (4) [redacted]			
STRUCTURE		**STRUCTURE**	
SUBSTANCE NAME	**CAS REG. NO.**	**SUBSTANCE NAME**	**CAS REG. NO.**
STRUCTURE		**STRUCTURE**	

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

(b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

(b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
(b) (4) [redacted]					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable. *See* the [redacted], reports in **Attachments 5-11** of [redacted] for residual analyses and validation of these analyses. *See* the [redacted] report in **Attachment 18** of [redacted] for the analyses of volatile compounds released from the FCS under microwave susceptor conditions of use. *See* **Attachments 1, 2, and 3** for LMWO data. *See* **Attachment 7** for additional data on the residual impurity [redacted]

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2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

As discussed in [redacted], a sample of the FCS was tested for residual monomers, oligomers, and for the presence of potential impurities. The fluoropolymer was dissolved in tetrahydrofuran (THF), and the resulting solution was analyzed for residual monomers and other potential impurities. The polymer was also analyzed using GPC to determine the percentage of low molecular weight oligomeric species. Residual amounts detected were provided in table II.B.3. of the Form 3480 for [redacted] and are repeated in table II.B.3 of this form for the convenience of the reviewer. Table II.B.3 of this form has also been revised to reflect the additional data provided in **Attachments 1, 2, 3 and 7.** Exposure estimates based on 100% migration of residuals are provided in **Attachment 8.** An example calculation, for NVP residual monomer follows:

1. The polymer is used at 1% in paper. (The product containing the polymer is used at 5%)
2. The basis weight of paper is 0.050 g/in^2
3. Migration from paper to food is 100%
4. 10 g of food will contact each square inch of paper

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The average residual level of NVP monomer is <0.5 parts per million (ppm or $\mu g/g$). Assuming 100% of the NVP will migrate to food: $(0.050\ g_{paper}/in^2)(0.0000005\ g_{NVP}/g_{FP})(0.05\ g_{[redacted]}/g_{paper})(0.2\ g_{FP}/g_{[redacted]})/(10\ g_{food}/in^2)$

$= 2.5 \times 10^{-11}\ g_{NVP}/g_{food}$, or 0.025 parts per billion (ppb).

Volatile Impurities Analysis (Microwave Susceptor Testing)

The volatiles identified in the headspace analysis of the FCS after heating with a microwave oven were assumed to be completely absorbed by the food. Our assumptions are very conservative, in that most of the volatiles are likely to remain in the headspace and not be absorbed by the food, which is removed from the microwave promptly after heating. Exposure estimates are provided in **Attachment 18** of [redacted] and employ the 0.001 consumption factor for microwave susceptor applications.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See **Attachment 8** for dietary concentration calculations for residual materials in the fluoropolymer FCS. As above, an example calculation, for NVP follows:

Given a CF of 0.05 for specialty paper, the dietary concentration for NVP is

0.025 ppb x 5% CF = 0.00125 ppb, or 0.00125 μg/kg

The EDI is 0.00125 μg/kg x 3 kg/p/d = 0.0038 μg/p/d

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2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

(b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Perfluorohexylethyl acrylate (13FA)	17527-29-6	0.2	0.01	0.03 µg/p/day	
1-Vinyl-2-pyrrolidone (NVP)	88-12-0	0.025	0.00125	0.0038 µg/p/day	
2-Hydroxyethyl methacrylate (HEMA)	868-77-9	0.44	0.02	0.06 µg/p/day	
Acrylic acid (AA)	79-10-7	1.0	0.05	0.15 µg/p/day	
Low-molecular weight oligomers	N/A	5.0	0.25	0.75 µg/p/day	
(b) (4)	(b) (4)	10.0	0.5	1.5 µg/p/day	
		50.0	2.5	7.5 µg/p/day	
		1.0	0.06	0.18 µg/p/day	
		6.3	0.3	0.9 µg/p/day	
		1.5	0.075	0.225 µg/p/day	
		50 ppt	2.5 ppt	0.0075 µg/p/day	
		0.45 ppt	0.022 ppt	0.000075 µg/p/day	
		0.5	0.03	0.09 µg/p/day	
		120 ppt	6 ppt	0.018 µg/p/day	
		5.0	0.3	0.9 µg/p/day	
See **Attachment 19** of (b) (4) for a summary of exposures to volatile byproducts and detailed exposure calculations.					

CONFIDENTIAL

Memorandum

Date January 7, 2011

From Division of Food Contact Notifications
Chemistry Review Team II

Subject FCN 001044 - Daikin America, Incorporated/Keller & Heckman. Submision dated 10–18-10 (received 10-19-10). Copolymer of C-6 fluoroacrylate, 1-vinyl-2-pyrrolidone, 2-hydroxyethyl methacrylate, and sodium acrylate as a grease-proofing agent for food-contact paper and paperboard.

To Division of Food Contact Notifications
Regulatory Team 1
Attn: M. Hepp, Ph.D.

Keller & Heckman, on behalf of Daikin America, Incorporated (DAI), has submitted food contact notification 1044 (FCN 001044) for the use of a copolymer of perfluorohexyethyl acrylate (aka C-6 fluoroacrylate (13 FA)), 2-hydroxyethyl methacrylate (HEMA), 1-vinyl-2-pyrrolidone (NVP) and sodium acrylate (NaA) at a level not to exceed 1.0 wt-% as a grease-proofing agent for food-contact paper and paperboard employed at the size press or wet-end in contact with all food types under conditions of use A - H and J (including microwave heat susceptor applications).

(b) (4) This FCS is not currently regulated nor has it been the subject of an effective FCN. There are numerous perfluoro-based, grease-proofing agents regulated or authorized for use in contact with food. The FCSs identified in Daikin's submission include FCNs 933, 888, 827 and 820, and are prepared from the same (FCNs 933 and 820) or a similar perfluoroalkylethylacrylate monomer.[1]

Identity

CAS Name: 2-propenoic acid, 2-methyl, 2-hydroxyethyl ester, polymer with 1-ethenyl-2-pyrrolidinone, 2-propenoic acid, and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl-2-propenoate, sodium salt

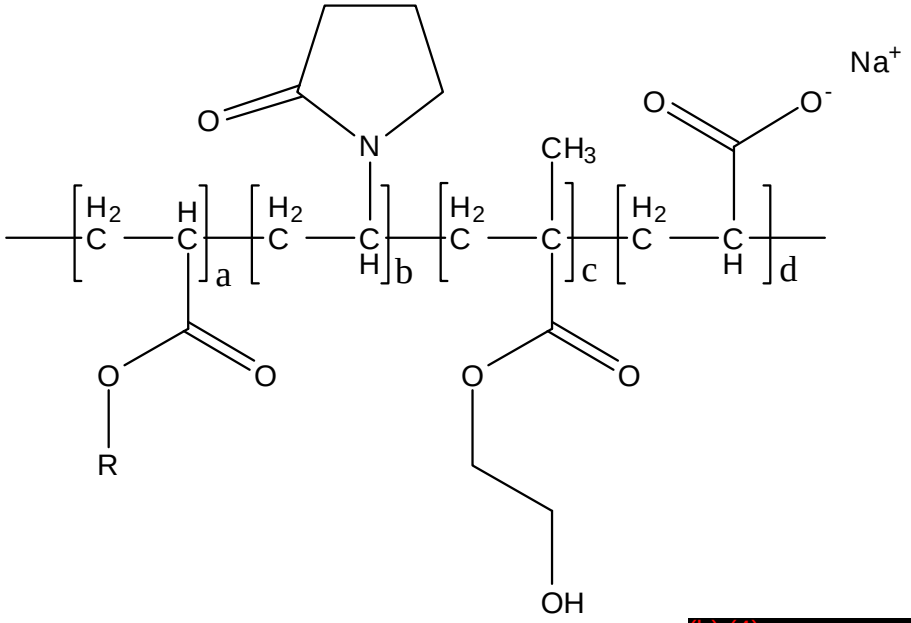
Other Names: copolymer of C-6 fluoroacrylate, 1-vinyl-2-pyrrolidone, 2-hydroxyethyl methacrylate and sodium acrylate

CAS Registry Number: 1206450-10-3

[1]See our chemistry memoranda dated 12/1/09 for FCN 933, dated 7/31/08 for FCN 827, and dated 7/1/08 for FCN 820 and the summary memorandum dated 5/27/10 for FCN 888.

Empirical Formula: (b) (4) [redacted]

Structure:



where R = $CH_2CH_2(CF_2)_5CF_3$ and the monomer mole ratios are: (b) (4) [redacted]

Infrared spectra of three lots of the FCS, which are consistent with its structure, are provided in Attachment 1 of (b) (4) [redacted]

Molecular Weight Distributions of the FCS

The notifier has provided three molecular weight (MW) studies of their FCS from two different laboratories. The MW distributions are tabulated below. In addition, the MW studies from (b) (4) [redacted] presented in (b) (4) [redacted] for the FCS and in FCNs 820 and 827 for similar FCSs are provided below for comparison.

Table 1. Gel Permeation Chromatography (GPC) Results for the FCS[2]

[2] M_n is the number-average MW, M_w is the weight-average MW, and PDI is the polydispersity index, which is the ratio of M_w to M_n.

Laboratory/Method/Solvent[3]	M_n (Da)	M_w (Da)	PDI	LMWO[4]
(b) (4) /GPC-RI/HFIP	(b) (4)			
(b) (4) /GPC-RI/HFIP				
(b) (4) /GPC-RI-MALLS/HFIP				
(b) (4) /GPC-MALLS-UV/THF (b) (4)				
(b) (4) /GPC-MALLS-UV/THF (FCN 820 - (b) (4))				
(b) (4) /GPC-MALLS-UV/THF (FCN 827 - (b) (4))				

(b) (4) GPC method with a refractive index detector (RI), utilizing poly(methyl methacrylate) (PMMA) standards to calibrate the GPC MWs and 0.005 M trifluoroacetic acid sodium salt in hexafluoroisopropanol (HFIP) as the mobile phase, is described in Attachment 1 of the FCN.[5] In addition (b) (4) utilized their GPC-RI method in concert with multi-angle laser light scattering detector (MALLS). Their GPC-MALLS method is described in Attachment 3 of the FCN.[6] (b) (4) utilized the same GPC-RI method as (b) (4) which is presented in Attachment 2 of the FCN.

The results clearly show that the (b) (4) results utilizing GPC-MALLS-UV presented in (b) (4) are an outlier. The earlier (b) (4) data utilizing GPC-MALLS-UV for the (b) (4) (FCN 820) and (b) (4) (FCN 827) exhibit the expected shape and the PDIs are closer to those of the current FCS.

[3]The three laboratories are (b) (4)

[4]LMWO is low MW oligomers having a MW of < 2000 Da.

[5]GPC-RI with MW calibration standards is the most commonly used form of GPC. While it provides an accurate MW distribution, the MWs depend on the similarity between the standards and the test polymer. The GPC column separates molecules according to size rather than molecular weight. Since a fluoroacrylate copolymer molecule has a higher MW than a PMMA molecule having the same size (because hydrogens are replaced with fluorine), MW results based on PMMA standard will be lower than the real MW of the fluoroacrylate copolymer.

[6]The MALLS detector provides absolute MWs, which will be more accurate than those obtained during GPC-RI with PMMA calibration standards when the test polymer is a fluoropolymer. Although the MALLS detector provides accurate MWs throughout the MW range of the polymer, it only measures accurate relative concentrations at high MWs. Hence, it is used with an RI or ultraviolet (UV) detector.

As stated in footnotes 4 and 5, the GPC-MALLS-RI data result in higher MWs than the corresponding GPC-RI data with PMMA calibration because the MALLS detector assigns absolute MWs to the signal to the RI detector, which measures relative concentrations. In contrast, because the GPC column separates substances according to size, rather than MW, use of the PMMA calibration only is valid if the MW of the tested polymer at a given RI signal corresponds to the MW at the same retention time obtained from the PPMA calibration standards. PMMA calibrations should yield more accurate MWs for polymers based on carbon, hydrogen, and oxygen than those obtained from monomers containing fluorine. Since a fluoroacrylate copolymer molecule has a higher MW than a PMMA molecule having the same size (because hydrogens are replaced with fluorine), MW results based on PMMA standard will be lower than the real MW of the fluoroacrylate copolymer.

Manufacture

(b) (4) [redacted]

Impurities

Non-Volatile

The residual levels of non-volatile starting materials (*i.e.*, 13 FA, HEMA, NVP, AA, (b) (4) [redacted]

(b) (4) [redacted]

(b) (4)

(b) (4) in the FCS are tabulated below.

Table 2. Residual Impurities in the FCS	
Migrant	Residual Level in FCS
13 FA	100 ppm
HEMA	128 ppm
NVP	< 0.5 ppm
AA	1065 ppm
(b) (4)	24 ppm
	131 ppm
	906 ppm
	20 ppm
	100 ppm
	203 ppm
	< 25 ppm
	51 ppm
	850 ppb
	8.5 ppb

The levels of 13 FA, (b) (4) in the FCS were determined using gas chromatography with a flame ionization detector (GC/FID) as described in Attachment 5 of (b) (4) High-pressure liquid chromatography with ultraviolet detection at 235 nm (HPLC/UV) was used to analyze for residual levels of NVP in the FCS (see Attachment 6 of (b) (4)). Levels of HEMA and AA in the FCS were determined using GC/FID (see Attachment 7 of (b) (4)). Liquid chromatography in tandem with mass spectrometry (LC -MS/MS) was used to analyze for levels of (b) (4) in the FCS (see Attachment 10 of (b) (4)

[8] (b) (4)

(b) (4)

(b) (4)

and Attachments 7-1 and 7-2 in FCN 1044). The residual levels of [redacted] were determined using GC/MS (see Attachment 8 of [redacted]). HPLC with UV detection at 290 nm was used to analyze for [redacted] in the FCS (see Attachment 9 of [redacted]). The level of [redacted] were determined using HPLC-MS as described in Attachment 11 of [redacted].

We note that the residuals level of some impurities (*i.e.*, 13 FA, HEMA, AA, [redacted]) reported in Table 1 do not all coincide with the values reported by the notifier. For example, the notifier reports the residual level of 13 FA to be < 4 ppm, where as it is reported above as 100 ppm.[11] Residual levels for each impurity were obtained by extraction of the FCS with an appropriate solvent. However, the method validation was not adequately performed in the instances of these impurities. While the *per cent* recoveries were acceptable, the level of spiking was well above the detected or non-detected level. For example, the notifier reports that 13 FA was not detected at < 4 ppm yet they spiked the FCS prior to any extraction with 100 ppm 13 FA with excellent recoveries. That proves that the method can detect with acceptable recoveries 100 ppm of 13 FA, but not 4 ppm 13 FA. Hence, < 100 ppm was used as the level of 13 FA in the FCS. In the absence of the proper method validation data, it is conservative to assume their spike level (with excellent recoveries) is the limit of detection of an impurity.[12]

Since [redacted] in monomers used to manufacture the FCS, they are present in the FCS. Both [redacted] are appropriately regulated for their intended use under 21 CFR 176.170 (Component of paper and paperboard in contact with aqueous and fatty foods). [redacted]

Volatile

The levels of volatile compounds released from the FCS upon microwave heating for 5 minutes at the highest power setting using headspace GC/MS are tabulated below. The method of analyses is described in Attachment 18 of the [redacted].

---

[11]The notifier reports the value for 13 FA, HEMA, AA, [redacted] as < 4 ppm, < 8.7 ppm, < 20 ppm, [redacted] respectively.

[12]We also note that in preliminary review we suggested to the notifier that if they wished to validate their method for the level of the analyte detected, they must spike the polymer prior to workup at the detected or non-detected level. Providing the validation would permit us to lower the exposure estimates to the five analytes. Since toxicology did not have a concern with exposure to each of the five analytes, using the higher residual levels, we did not request that the notifier provide the validation for the detected or non-detected level of each analyte.

Table 3. Volatile Migrants for the FCS Upon Microwave Heating	
Migrant	Migration
(b) (4)	0.792 µg/in^2
	0.065 µg/in^2
	0.026 µg/in^2
	0.010 µg/in^2
	0.028 µg/in^2
	4.94 µg/in^2
	0.007 µg/in^2
	0.049 µg/in^2
	0.043 µg/in^2
	0.019 µg/in^2
	0.081 µg/in^2

Intended Use/Technical Effect

The FCS is intended to be used as a grease-proofing agent for food-contact paper and paperboard employed either prior to the sheet forming operation (i.e., wet-end) or at the size press. The FCS will be used at a level not to exceed 1 wt.-% (dry) of the food-contact paper and paperboard. ((b) (4)) The FCS may contact all food under conditions of use A through H and J (microwave susceptor applications).

Stability

The notifier states that the FCS is stable under their proposed conditions of use. A thermogravimetric analysis of the FCS is provided in Attachment 17 of (b) (4) .

Migration/Exposure

Non-Volatile Migrants

Migration testing was not conducted for the non-volatile migrants contained in the FCS. Instead, the notifier performed residue analysis for LMW oligomers and impurities in the

finished FCS.[13] The migration of and exposure to LMW oligomers and impurities from the proposed uses of the FCS is calculated based on 100% migration.

For condition of use A-H, the concentration in food (<M>) of the LMW oligomers and each impurity is determined by multiplying the residual level in the FCS by the basis weight of paper (0.05 g/in^2), by the level of the FCS in the product (0.2 g FCS/g (b) (4)), by the level of (b) (4) added to the paper (0.05 g (b) (4) /g paper) and dividing by the food contact to surface area ratio (10 g/in^2). The dietary concentration (DC) of the LMW oligomers and each impurity is calculated by multiplying the <M> by the consumption factor (CF) of 0.05 for specialty paper. The estimated daily intake (EDI) of the LMW oligomers and each impurity is calculated by multiplying the DC by the daily diet of 3000 g food /person/day.

For the microwave susceptor use, the <M> of the LMW oligomers and each impurity is determined by multiplying the residual level in the FCS by the basis weight of paper for microwave use (0.023 g/in^2), by the level of the FCS in the product (0.2 g FCS/g (b) (4)), by the level of (b) (4) added to the paper (0.05 g (b) (4) /g paper) and dividing by the food contact to surface area ratio (0.52 g/in^2). (The food contact to surface area ratio of 0.52 g/in^2 was determined based on the microwave popcorn bag being the worst-case use for a grease-proofing agent in a heat susceptor (b) (4)). The DC of the LMW oligomers and each impurity is calculated by multiplying the <M> by the CF of 0.001 for microwave heat susceptors. The EDI of the LMW oligomers and each impurity is calculated by multiplying the DC by the daily diet of 3000 g food /person/day.

The residual level of the LMW oligomers and impurities, their <M>, and exposure is tabulated below.

[13]See the section on *Molecular Weight Distribution of the FCS* for the details in determining the LMW oligomers (< 2000 g/mole; (b) (4)) of the FCS (see Table 1) and on Impurities for the details in determining the residual level of impurities (see Table 2).

Table 4. Residual Impurities, Their Migration, and Exposure from the Proposed Use of the FCS				
Migrant	Residual Level	<M> A-H; microwave	DC A-H + microwave	EDI combined
oligomers	100 ppm	5.0 ppb; 96 ppb	0.25 ppb + 44 pptr	0.87 µg/p/d
perfluorohexylethyl acrylate (13 FA)	100 ppm	5.0 ppb; 96 ppb	0.25 ppb + 44 pptr	0.87 µg/p/d
2-hydroxyethyl methacrylate (HEMA)	128 ppm	6.4 ppb; 123 ppb	0.32 ppb + 57 pptr	1.1 µg/p/d
1-vinyl-2-pyrrolidone (NVP)	< 0.5 ppm	25 pptr; 0.48 ppb	1.3 pptr + 0.22 pptr	4.5 ng/p/d
acrylic acid (AA)	1065 ppm	53 ppb; 1024 ppb	2.7 ppb + 0.47 ppb	9.6 µg/p/d
(b) (4)	24 ppm	1.2 ppb; 23 ppb	60 pptr + 11 pptr	0.21 µg/p/d
	131 ppm	6.6 ppb; 126 ppb	0.33 ppb + 58 pptr	1.2 µg/p/d
	906 ppm	45 ppb; 871 ppb	2.3 ppb + 0.40 ppb	8.1 µg/p/d
	20 ppm	1.0 ppb; 19 ppb	50 pptr + 8.8 pptr	0.18 µg/p/d
	100 ppm	5.0 ppb; 95 ppb	0.25 ppb + 44 pptr	0.87 µg/p/d
	203 ppm	10 ppb; 195 ppb	0.5 ppb + 90 pptr	1.8 µg/p/d
	2.4 ppm[14]	0.12 ppb; 2.3 ppb	6 pptr + 1.0 pptr	21 ng/p/d
	51 ppm	2.6 ppb; 49 ppb	0.13 ppb + 23 pptr	0.45 µg/p/d
	850 ppb	43 pptr; 0.8 ppb	2.1 pptr + 0.4 pptr	7.5 ng/p/d
	8.5 ppb	0.43 pptr; 8.2 pptr	0.021 pptr + 3.8 ppqd	75 pg/p/d

Volatile Migrants

Migration testing was conducted for volatile migrants from the FCS upon microwave heating for 5 minutes at the highest power setting using headspace GC/MS as described in Attachment 18 of the (b) (4). The migration of each of the volatile impurities is tabulated in Table 3.

(b) (4)

For the microwave susceptor use, we assume all the volatile impurities would migrate into the food.[15] The <M> for each impurity is calculated by dividing the migration from the FCS (in µg/in^2) by the food contact to surface area ratio (0.52 g/in^2). (The food contact to surface area ratio of 0.52 g/in^2 was determined based on the microwave popcorn bag being the worst-case use for a grease-proofing agent in a heat susceptor (b) (4) [redacted] The DC for each impurity is calculated by multiplying the <M> by the CF of 0.001 for microwave heat susceptors. The EDI for each impurity is calculated by multiplying the DC by the daily diet of 3000 g food /person/day.

The migration level and exposure to the volatile migrants from the proposed use of the FCS in microwave heating is tabulated below.

Table 5. Exposure to Volatile Migrants from the Proposed Use of FCS in Microwave Susceptors

Migrant	Migration	DC	EDI
(b) (4) [redacted]	0.792 µg/in^2	1.5 ppb	4.5 µg/p/d
	0.065 µg/in^2	0.13 ppb	0.39 µg/p/d
	0.026 µg/in^2	50 pptr	0.15 µg/p/d
	0.010 µg/in^2	19 pptr	57 ng/p/d
	0.028 µg/in^2	54 pptr	0.16 µg/p/d
	4.94 µg/in^2	9.5 ppb	28 µg/p/d
	0.007 µg/in^2	13 pptr	39 ng/p/d
	0.049 µg/in^2	94 pptr	0.28 µg/p/d
	0.043 µg/in^2	83 pptr	0.25 µg/p/d
	0.019 µg/in^2	36 pptr	0.11 µg/p/d
	0.081 µg/in^2	0.16 ppb	0.48 µg/p/d

[15]This assumption is conservative in that most of the volatile migrants will remain in the headspace gasses and not be absorbed by the food, which is removed from the microwave promptly after heating.

Cumulative Exposure

C6-Based Perfluoro Oligomers

There are currently seven effective FCNs for perfluoro polymers structurally similar to the FCS with side chains containing six perfluorinated carbon atoms: FCNs 542, 599, 604, 820, 827, 888, and 933. A review of the chemistry memoranda for FCNs 542, 599, 604, 827, 888, and 933 indicates that the exposure to C6 oligomers from these FCNs is 0.5 ppb, 0.5 ppb, 10 pptr, 0.4 ppb, 7.4 pptr, and 0.08 ppb, respectively. As these calculations are based on the CF for specialty paper and 100% market capture, and their intended uses are substitutional (conditions of use A - H and J (microwave susceptor use)), the total DC to C6 oligomers from these FCNs would be 0.5 ppb.[16] (b) (4) [redacted] and a review of chemistry memorandum for this FCN indicates a DC of 0.5 ppb. Since we do not have data that would permit us to estimate the fraction of market capture by each of these related FCSs, we must assume that the exposure would be additive. As such, a conservative estimate for the cumulative DC (CDC) of the C6 oligomers would be 0.5 ppb from FCNs 542, 599, 604, 827, 888, and 933, plus 0.5 ppb from FCN 820, or 1.0 ppb. The DC of 0.39 ppb (or 0.25 ppb + 44 pptr) for the C6 oligomers from the use of the FCS in this FCN would be subsumed by CDC of 1 ppb for C6 oligomers.

(b) (4) [redacted]

Other CDCs

Given the low DCs for the impurities and the substitutional use of the FCS, we believe that they would not contribute to their respective cumulative CDCs. Therefore, there will be no

[16]FCN 542 and 599 covers conditions of use B - H. FCN 827 covers conditions of use A -H. FCN 604 covers conditions of use J (microwave susceptor use). FCNs 888 and 933 cover conditions of use A-H and J (microwave susceptor use).

[17]The total DC for the FCS in FCN 933 was 0.07 ppb for conditions of use A -H and 2.2 ppb for the condition of use J (microwave susceptor use).

change in their CDCs.

Notification Language

The acknowledgment letter, as signed by chemistry on 11-15-10, is appropriate as written.

Summary

We have no questions.

Roseann M. Costantino, Ph.D.

HFS-275, R/F
HFS-275:RMCostantino:FCN 001044.wpd:1-5-11
R/DInit:HFS-275:MAAdams:1-7-11
Final:maa:1-7-11

change in their CDCs.

Notification Language

The acknowledgment letter, as signed by chemistry on 11-15-10, is appropriate as written.

Summary

We have no questions.

(b) (6)

[redacted]

Roseann M. Costantino, Ph.D.

HFS-275, R/F
HFS-275:RMCostantino:FCN 001044.wpd:1-5-11
R/DInit:HFS-275:MAAdams:1-7-11
Final:maa:1-7-11

Memorandum

Date: June 9, 2014

From: Division of Food Contact Notifications
Chemistry Review Group II
Roseann M. Costantino, Ph.D.

Subject: FCN 001044 – Daikin America, Incorporated/Keller & Heckman. Correction of cumulative dietary concentration of (b) (4).

To: Division of Food Contact Notifications
Regulatory Team II
Attn: A. Lipman, Ph.D.

Keller and Heckman, on behalf of Daikin America, Incorporated, submitted food contact notification 1044 (FCN 001044) for the use of a copolymer of perfluorohexyethyl acrylate (aka C-6 fluoroacrylate (13 FA)), 2-hydroxyethyl methacrylate (HEMA), 1-vinyl-2-pyrrolidone (NVP) and sodium acrylate (NaA) (FCS) at a level not to exceed 1.0 wt-% as a grease-proofing agent for food-contact paper and paperboard employed at the size press or wet-end in contact with all food types under conditions of use A - H and J (including microwave heat susceptor applications). This FCN became effective on February 16, 2011.

This memorandum is written to correct the cumulative dietary concentration (CDC) of (b) (4), as presented in our chemistry memorandum dated 1-7-11. In addition, we note that Table 4 of that memorandum has incorrect values for the concentration in food (<M>) of the migrants from the microwave use of the FCS. These corrections are presented below.

Revised CDC

(b) (4)

Revised <M> for Microwave Use of the FCS

While page 8 in the second complete paragraph accurately describes the calculation for determining the <M> of the migrants from the microwave use of the FCS, the values for the

(b) (4)

<M> of the migrants from the microwave use of the FCS in Table 4 on page 9 were determined using a basis weight of paper of 0.05 g/in^2, instead of 0.023 g/in^2 (the basis weight of paper for microwave use). The revised <M> for each migrant from the microwave use of the FCS are provided in bold typeface below. The values for residual levels, <M> of the migrants from condition of use A-H of the FCS, the DCs and the EDIs remain unchanged.

Table 4. Residual Impurities, Their Migration, and Exposure from the Proposed Use of the FCS

Migrant	Residual Level	<M> A-H; microwave	DC A-H + microwave	EDI combined
oligomers	100 ppm	5.0 ppb; **44 ppb**	0.25 ppb + 44 pptr	0.87 µg/p/d
perfluorohexylethyl acrylate (13 FA)	100 ppm	5.0 ppb; **44 ppb**	0.25 ppb + 44 pptr	0.87 µg/p/d
2-hydroxyethyl methacrylate (HEMA)	128 ppm	6.4 ppb; **57 ppb**	0.32 ppb + 57 pptr	1.1 µg/p/d
1-vinyl-2-pyrrolidone (NVP)	< 0.5 ppm	25 pptr; **0.22 ppb**	1.3 pptr + 0.22 pptr	4.5 ng/p/d
acrylic acid (AA)	1065 ppm	53 ppb; **471 ppb**	2.7 ppb + 0.47 ppb	9.6 µg/p/d
(b) (4)	24 ppm	1.2 ppb; **11 ppb**	60 pptr + 11 pptr	0.21 µg/p/d
	131 ppm	6.6 ppb; **58 ppb**	0.33 ppb + 58 pptr	1.2 µg/p/d
	906 ppm	45 ppb; **401 ppb**	2.3 ppb + 0.40 ppb	8.1 µg/p/d
	20 ppm	1.0 ppb; **8.8 ppb**	50 pptr + 8.8 pptr	0.18 µg/p/d
	100 ppm	5.0 ppb; **44 ppb**	0.25 ppb + 44 pptr	0.87 µg/p/d
	203 ppm	10 ppb; **90 ppb**	0.5 ppb + 90 pptr	1.8 µg/p/d
	2.4 ppm	0.12 ppb; **1.0 ppb**	6 pptr + 1.0 pptr	21 ng/p/d
	51 ppm	2.6 ppb; **23 ppb**	0.13 ppb + 23 pptr	0.45 µg/p/d
	850 ppb	43 pptr; **0.4 ppb**	2.1 pptr + 0.4 pptr	7.5 ng/p/d
	8.5 ppb	0.43 pptr; **3.8 pptr**	0.021 pptr + 3.8 ppqd	75 pg/p/d

Roseann M. Costantino -S

Digita ly signed by Roseann M Costantino S
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ou=FDA ou=People
0.9 23.42 19200300 100 1 1=1300065330
cn=Roseann M Costantino S
Date: 2014 06 09 08:20 12 04 00

Roseann M. Costantino, Ph.D.

HFS-275, R/F
HFS-275:RMCostantino:FCN 001044a.docx:6-4-14
R/DInit:KBArvidson:6-5-14
Final:rmc:6-9-14

CH

Equivalency of Migration Obtained under Condition of Use H

to Migration Obtained under Condition of Use C

Equivalency can be shown using accepted principles of diffusion.

In the case where a given migrant is present in the food-contact layer, migration into food at a time t is given by:[1]

$$M_t = 2 * C_{p0} * \rho * (D_p t/\pi)^{1/2} \qquad (1)$$

where M_t is migration at time t, C_{p0} is the initial concentration of the migrant in the polymer ρ is the density of the polymer, and D_p is the diffusion coefficient of the migrant in the polymer. The equation is valid provided that (1) the migrant concentration in the polymer does not change significantly over time and (2) the food is an infinite "sink" for the migrant with no significant resistance to mass transfer. D_p, the diffusion coefficient, can be estimated using the semiempirical equation developed by Baner *et al.*:[2]

$$D_p = 10^4 * \exp(A_p - a * M_r - b * T^{-1}) \qquad (2)$$

where D_p is the diffusion coefficient, A_p accounts for the effect of the polymer on diffusivity, M_r is the substance's molecular weight, T is the temperature in degrees Kelvin, and a and b are correlation constants for molecular weight and temperature effects on diffusion, with values 0.10 and 10450, respectively. For example, the current A_p values for poly(ethylene terephthalate) and low density polyethylene are –3 and +9, respectively. Although A_p for fluoropolymers is not known, there is a "default" A_p of 0 for "other polymers." From examination of (2), it can be seen that the smaller the A_p and the higher the molecular weight, the smaller will be the diffusion constant and the lower the migration.

Specific inputs to the two equations are the following:

1. **A_p:** As noted, the value for "other polymers" is 0.

2. **Time (t) and temperature (T):** FDA's Guidance document specifies two protocols for Condition of Use C. The first is 100°C for 30 minutes, followed by 40°C to 10 days. The second is 66°C for two hours, followed by 40°C to 10 days. Because the basic diffusion equation does not account for changing temperatures, the conservative assumption is made that the migration value obtained at the higher temperature can be added to the migration value at the lower temperature to give the total migration value.

3. **C_{p0}:** To estimate C_{p0} for oligomers we need to estimate the fraction of the polymer that is able to migrate. However, since we are comparing relative

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[1] Crank, J. *The Mathematics of Diffusion*, Clarendon Press: Oxford, UK, 1975.

[2] Baner, A., Brandsch, J., Franz, R. and Piringer, O. (1996). The applications of a predictive migration model for evaluating the compliance of plastic materials with European food regulations. *Food Additives & Contaminants* **13(5)**, 587-601.

[redacted]

migration values, *i.e.*, migration from application of FDA's protocol for Condition of Use C is compared to migration after 2 hours at 100°C (Condition of Use H), the choice of C_{p0} is arbitrary. For our calculation we selected 0.01%, but any value would result in the same qualitative conclusion.

Using the Crank equation, migration from a polymer having $A_p = 0$ after 2 hours at 100°C was compared with migration under both of FDA's recommended protocols for Condition of Use C: (a) 100°C for 30 minutes, followed by 40°C for a total of 240 hours, and (b) 66°C for 2 hours, followed by 40°C for a total of 240 hours. Diffusion coefficients for two different molecular weights are tabulated in Table 1. Corresponding migration values are calculated in Table 2.

Table 1

Diffusion Coefficients (cm^2/sec)

Temperature (°C)	150 daltons	500 daltons
100	9.1×10^{-11}	4.6×10^{-11}
66	1.5×10^{-9}	2.8×10^{-12}
40	7.1×10^{-12}	2.1×10^{-13}

Table 2

Calculated Migration in PPM
($C_{p0} = 0.01\%$)

Protocol	150 daltons	500 daltons
100°C for 2 hours	0.24 ppm	0.042 ppm
100°C for 30 minutes + 40°C for 240 hours	0.30 ppm	0.052 ppm
66°C for 2 hours + 40°C for 240 hours	0.24 ppm	0.041 ppm

Comments

1. Although the Fluorolink F10 polymer is not applied as a continuous coating, but is embedded in the paper article, the diffusion equation makes no distinction between the two cases. The equation is conservative in that a polymer film having infinite thickness is assumed.

2. As shown in Table 2, migration after 2 hours at 100°C is virtually identical to migration after 2 hours at 66°C followed by migration for 10 days at 240 hours. Predicted migration after 2 hours at 100°C is lower than migration after 30 minutes at 100°C followed by 240 hours at 40°C. However, as stated above, the calculations were performed using the assumption that migration at the higher temperature for a specified

time period can simply be added to 240 hour migration at a lower temperature. This is an exaggeration forced on us by the simple equation used. Clearly, migration at the higher temperature will result in a lower migration potential for subsequent migration at 40°C because a higher percentage of the initial concentration will be depleted after migration at the higher temperature. A more accurate calculation would have to explicitly include polymer thickness in order to account for declining concentrations (C_{p0}) as migration progressed. Given the similarity of the results among the three protocols, such a level of complexity is not warranted.

We conclude that migration obtained after 2 hours at 100°C should not differ significantly from migration obtained under either of FDA's two protocols for Condition of Use C.

FDA's Statement (Anna P. Shanklin, 12/5/01):

"The manufacturer should provide an explanation for their statement in Section F (p.12) that, 'the LC-MS method used in the analysis of Fluorolink F10 in extracts from treated paper would also quantitate the precursor.' We ask that their explanation point to specific place[s] in their data submission that would illustrate this point. This information is needed for the evaluation of the exposure estimate for ethoxylated perfluoroether diol."

Response:

The mass spectrometer detector was set to select masses (m/Z) between 900 and 1700 daltons. Since the ethoxylated perfluoroether diol has a molecular weight distribution that partially falls within that range, as does Fluorolink F10, it would produce a signal on the HPLC chromatogram if it were to pass into the detector.[1] Also, since the precursor and Flurolink F10 are structurally similar, it is likely that ethoxylated perfluoroether diol would also elute on the same HPLC column under the same conditions as for Fluorolink F10. However, in the absence of data showing conclusively that the retention times would overlap or that the response factors would be similar, it nevertheless can be shown that even if the precursor is present at 5% as an unreacted residual in Fluorolink F10, the dietary concentration of the toxicologically significant fraction, (*i.e.*, the fraction of the polymer not exceeding 1000 daltons), is safe.

The gel permeation chromatograph of ethoxylated perfluoroether diol (Z-DOL TX) is provided in Appendix II. From examination of the accompanying slice table, it is apparent that less than 2% of the polymer has molecular weight under 1000 daltons. Assuming that Fluorolink F10 is present in paper at a maximum level of 1.5% and the precursor is present in Fluorolink F10 at a maximum 5%, 100% migration of the fraction under 1000 daltons from paper having basis weight 0.050 g/in^2, would be:

$(0.015\ g_{F10}/g_{paper})(0.05\ g_{ZDOL\ TX}/g_{F10})(0.02\ g_{lmwf}/g_{ZDOL\ TX})(0.050\ g_{paper}/in^2)/(10\ g_{food}/in^2) = 7.5 \times 10^{-8}\ g_{lmwf}/g_{food}$, or 75 ppb.

Applying the 0.10 consumption factor for uncoated paper results in a maximum dietary concentration of 7.5 ppb. The EDI would be 22.5 μg/person/day. Ethoxylated perfluoroether diol tested negative in the Ames assay (see accompanying submission), and neither its precursor, perfluoroether diol, nor its reaction product, Fluorolink F10, are genotoxic (see Appendices V and IV, and submission of November 27, 2001 to Sandra Varner).

In order to provide a more accurate estimate of potential exposure, TNO analyzed Fluorolink F10 for ethoxylated perfluoroether diol using a normal phase HPLC procedure employing gradient elution.[2] Ethoxylated perfluoroether diol was found to be present at 0.67% in Fluorolink F10. Therefore, a more realistic, but still conservative, estimate of exposure would

[1] As shown in Appendix III, the average molecular weight of perfluoroether diol is 1500 daltons.

[2] Eluting solvents were (A) tetrahydrofuran with 0.1% trifluoroacetic acid (TFA), (B) heptane, and (C) heptafluoroisopropanol (HFIP) with 0.1% TFA. The sample was injected as an HFIP solution. The HPLC detector was an evaporative light scattering detector. The report from TNO is attached.

[redacted]

be 0.134 times that calculated above.[3] One hundred percent migration of the fraction under 1000 daltons would be 10 ppb, and the dietary concentration would be 1 ppb. The EDI would be 3 μg/person/day. Even if the entire polymer were to migrate, the dietary concentration would not exceed 50 ppb.[4]

Therefore, Ausimont respectfully submits that the presence of ethoxylated perfluoroether diol as an impurity in Fluorolink F10 poses no safety issue.

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3 (0.67) (5.0) = 0.134

4 $[(0.015\ g_{F10}/g_{paper})(0.0067\ g_{ZDOL\ IN}\ g_{F10})\ (0.050\ g_{paper}/in^2)/(10\ g_{food}/in^2)](0.10) = 5.0 \times 10^{-8}\ g_{ZDOL\ IN}\ g_{diet} =$ 50 ppb

[redacted]

SOLENIS FCN 314

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2. CAS Registry Number

464178-90-3

3. Trade or Common Name

D-1085

4. Other Chemical Names (IUPAC, etc.)

n/a

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

See Attachment 1 for chemical structure. The chemical formula is:

$H\text{-}(C_2H_5N)_{x1}\text{-}(C_5H_{11}NO_2)_{x2}\text{-}(C_5H_{10}NOCl)_{x3}\text{-}(C_5H_9NOCl)_{x4}\text{-}(C_5H_{10}NON\text{-x link})_{x5}\text{-}(C_{11\text{-}23}H_{10}NOF_{13\text{-}37})_{x6}\text{-}(C_8H_{17}NO_3Cl)_{x7}\text{ -}C_{12\text{-}24}H_{12}N\text{-x link}F_{13\text{-}37}$

(b) (4) [redacted]

(b) (4) [redacted]

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

^{13}C NMR and ^{1}H NMR spectra are included in Attachment 2

000007

Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

[redacted]

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
Mix of perfluoralkyl iodides	25398-32-7	Starting material
Allyl alcohol	107-18-6	Starting material
Potassium hydroxide	1310-58-3	Reagent
Triethylenetetramine	112-24-3	Starting material
Epichlorohydrin	106-89-8	Starting material
[redacted]		
Water	7732-18-5	Solvent

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See Attachment 3 for manufacturing information.

000008

[redacted]

Section B - MANUFACTURE - Continued

(b) (4) [redacted]

5. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (dry basis)	Maximum Residual (%)
Flourinated telomer iodide starting material (Zonyl TELA-N)	25398-32-7	(b) (4) [redacted]	
Allyl alcohol	107-18-6		
Fluorinated iodohydrin intermediate	38550-44-6 38550-45-7 38550-46-8 80459-24-1		
Tetramethyl succinonitrile	3333-52-6		
(b) (4) [redacted]			
(b) (4) [redacted]			
Epichlorohydrin	106-89-8		
2,3-Dichloro-1-propanol	616-23-9		
1,3-Dichloro-1-propanol	96-23-1		
3-Chloro-1,2-propanediol	96-24-2		
Triethylenetetramine	112-24-3		

** As described on page 116 of the migration report in Attachment 7, each of these impurities is made up of a range of congeners. In each case, the C_8 is the most abundant, constituting one-half or more of the various congeners. Therefore, if the C_8 is not detected in residual analyses, the other congeners will also not be detected. For this reason, the C_{10} and C_{12} congeners were not necessarily included on the chromatograms provided. Nonetheless, rather than taking one-half of the detection limit for each species in our 100% migration calculations, we are using the detection limit amount so as to include all the congeners.

000009

Ensure that exposures to these substances are addressed in Section II.G of this form.

(b) (4) [redacted]

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A 5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications. (b) (4) [redacted]

Property	Max. Value	Min. Value	Individual Batch Values
pH (Hercules IM 443-4 method)	6 3	3 5	4.9 4.9 4.9
Wt % total solids (Hercules IM 443-2 method)	21.0	19 0	19.6 19.5 19.8
Brookfield viscosity (cps, 22-23°C) (Hercules IM 443-3 method)	800	200	400 290 300
			000010
Test methods are provided in Attachment 4			(b) (4) [redacted]

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Weight percent polymer below 1000 Daltons = 3%
Weight percent polymer below 500 Daltons is not available

(See Attachment 7, pp. 9, 128-140)

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard at levels up to 0.5% by weight of the dry paper and paperboard intended for use in contact with food. Single use of the food-contact material is anticipated.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

000011

Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
FCS in paper and paperboard up to 0.5% by weight of the dry paper and paperboard	All food types (Types I – IX)	B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

000012

Part II — CHEMISTRY INFORMATION - CONTINUED

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil/grease/fat and water stains can weaken paper, making it susceptible to punctures and tears. In addition, the stains hurt the print quality of the paper and can make the bag appearance undesirable to the consumer. When the oil/grease/fat or water contained in the paper bag/container wets the outer surface of the bag/container, the surfaces the paper comes in contact with can become slippery, creating a safety hazard. Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water.

Data demonstrating the technical effect of the FCS are provided in Attachment 6. Three different types of tests were conducted (Kit number, Pet Food Test, and HST), comparing the FCS to four of the leading commercial products in the market. Three batches of the FCS, as well as an untreated paper control, were compared to these commercial products.

The minimum amount needed to achieve the intended technical effect is 0.05% - 0.5%.

Section E - STABILITY DATA

See Chemistry Recommendations Section II D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

000013

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

000014

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D 5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

The test specimens used in the migration study consisted of commercially prepared sheets weighing 50 lbs/3000 ft^2. This is equivalent to 52 4 mg paper/in^2 (50 lbs x 453 g/lb x 1000 mg/g ÷ 3000 ft^2 ÷ 144 in^2/ft^2 = 52.4 mg/in^2). Untreated sheets were used as controls, and treated sheets were prepared containing 0.5% by weight of the FCS. For 1,3-DCP and CPD, the FCS was added to the samples prior to the sheet-forming operation. For all other analytes, the FCS was applied to the samples as a surface treatment. The FCS used to prepare the treated sheets contained the impurities and their respective concentrations found in Part II, Item 1 of this FCN (page 5). The residual levels of these impurities were not determined in the treated test specimens. The treated test specimens and control specimens were immersed in the food simulating solvents

A copy of the migration study report is included in Attachment 7.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred. (b) (4) [redacted]

The aqueous food simulant (10% ethanol) and fatty food simulants (corn oil and 50% ethanol) were exposed to both sides of the sample and control sheets at a volume-to-surface area ratio of 2 mls/in^2 (1-side area). No turbidity or precipitation was observed in the sample extracts. Aliquots of the control and sample extracts were analyzed at 2, 24, 96, and 240 hours for 1,3-DCP and 3-CPD, and at 2 and 240 hours for (b) (4) [redacted], TETA, and (b) (4) [redacted]. The 24 and 96 hour extracts were not analyzed since (b) (4) [redacted] TETA, and (b) (4) [redacted] were not detected after 2 and 240 hours using a method sensitivity of 5 ppb, 1 ppb, and 10 ppb, respectively.

000015

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in² 0.011 mg/in² 0.021 mg/in²	0.015 mg/in²
			40°C analysis after 24 hours	0.015 mg/in² 0.014 mg/in² 0.022 mg/in²	0.017 mg/in²
			40°C analysis after 96 hours	0.017 mg/in² 0.017 mg/in² 0.023 mg/in²	0.019 mg/in²
			40°C analysis after 240 hours	0.020 mg/in² 0.021 mg/in² 0.023 mg/in²	0.021 mg/in²

000016

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food/Food Simulant	Temp/time of analysis	Migration ($\mu g/in^2$)			Avg. ($\mu g/in^2$) Migration
50 lb/3000 ft^2 uncoated paper sheets treated at 0 5% dry weight FCS	1,3-DCP	10% ethanol	100° C; analysis after 2 hours	0.00014	0.00015	0.00017	0.00015
			40° C; analysis after 24 hours	0.00030	0.00040	0.00027	0.000326
			40° C; analysis after 96 hours	0.00030	0.00026	0.00027	0.000273
			40° C; analysis after 240 hours	0.00024	0.00014	0 00020	0.00019
		Corn oil	100° C; analysis after 2 hours	<0.00035	<0.00035	<0.00035	<0.00035
			40° C, analysis after 24 hours	<0.00035	<0.00035	<0.00035	<0.00035
			40° C; analysis after 96 hours	<0.00035	<0.00035	<0.00035	<0.00035
			40° C; analysis after 240 hours	<0.00043	<0.00043	<0.00043	<0.00043
	3-CPD	10% ethanol	100° C; analysis after 2 hours	0.00131	0.00150	0.00184	0.001546
			40° C, analysis after 24 hours	0.00141	0.00238	0.00265	0.00214
			40° C; analysis after 96 hours	0.00235	0.00242	0.00197	0.00225
			40° C; analysis after 240 hours	0.00152	0.00174	0.00156	0.00161
		Corn oil	100° C; analysis after 2 hours	0.00090	0.00060	0.00044	0 0004
			40° C; analysis after 24 hours	0 00269	0.00241	0 00256	0.0001
			40° C; analysis after 96 hours	0.00580	0.00568	0.00664	0.0007
			40° C; analysis after 240 hours	0.01204	0.01348	0.01443	0.0018
[redacted] (b) (4)	[redacted] (b) (4)						
	TETA	10% ethanol	100° C; analysis after 2 hours	<0.01	<0.01	<0.01	<0.01
		10% ethanol	40° C; analysis after 240 hours	<0.01	<0.01	<0.01	<0.01
		50% ethanol	100° C; analysis after 2 hours	<0.01	<0.01	<0.01	<0.01
		50% ethanol	40° C; analysis after 240 hours	<0.01	<0.01	<0.01	<0.01

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Analyte	10% Ethanol			Corn oil/50% Ethanol		
	Amount added (ug/in^2)	% Recovery	% RSD	Amount added (ug/in^2)	% Recovery	% RSD
1,3-DCP	0.00015	Detected	-	0.0024	Detected	-
	0 0015	34	15	0.0040	64	12
	0.0057	20	8.5	0.0080	61	4.6
3-CPD	-	-	-	0.010	95	0.96
	0.10	84	6.0	0.025	90	13
	0.50	86	4.8	0.050	84	0.89
	1.0	79	6.5	0.10	90	17
(b) (4)						
TETA	0.10	Detected	-	0.10 (50% ethanol)	Detected	-

(b) (4)

(b) (4)

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

The following calculations utilize the residual levels provided in Part II, B, 3, and assume (1) 50 mg paper/in^2 treated with 0.5% FCS, and (2) 100% migration to 10 g food/in^2.

FCS

See Attachment 7, p. 9 for explanation of maximum oligomer migration level.
50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000410 mg oligomers/mg FCS ÷ 10,000 mg food/in^2 = 1.03 x 10^{-8} mg oligomers/mg food = 10.3 ppb

IMPURITIES

For the impurities listed below, we also assume that 98% of the substances go out with the white water and 2% stay with the paper:

(b) (4)

Section G- ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

(b) (4)

One-half the sensitivity level is used below as the maximum level of migration where a substance was not detected at a given sensitivity, and where the chromatography supports the use of one-half the detection limit. In addition, all migration values in µg/in^2 were converted to µg/kg food (ppb) as follows. µg/in^2 – 0 01 kg food/in^2 = µg/kg. A consumption factor (CF) of 5% for specialty paper and the food type distribution factors for uncoated paper (59% aqueous, 41% fatty) are used below to calculate the EDI for each substance.

In addition, since the migration studies for (b) (4), TETA, and the (b) (4) were done on paper prepared by size press addition of the FCS, and since wet-end addition results in only 2% of the non-substantive material remaining with the finished paper and migration is a function of concentration, we are taking 2% of the measured migration values (or ½ the detection limit, where appropriate) to represent wet-end addition.

TETA = 0 05 CF x 0 5 µg/kg x 0 02 x 3 kg/p/d (b) (4) = 0 0015 µg/p/d

(b) (4)

(b) (4)

The migration studies on the remaining analytes were done on paper prepared by wet-end addition. Thus, the values below are as reported in the migration studies:

1,3-DCP = 0 05 CF x [(0.59) (0 0326 µg/kg) + (0 41)(0.043 µg/kg)] x 3 kg/p/d = 0.0055 µg/p/d
3-CPD = 0.05 CF x [(0.59) (0 23 µg/kg) + (0.41)(0.18 µg/kg)] x 3 kg/p/d = 0.0314 µg/p/d

The remaining dietary exposure calculations are based on 100% migration calculations provided in Section F(2).

Oligomers = 0.05 CF x 10 3 µg/kg x 3 kg/p/d = 1.55 µg/p/d

(b) (4)

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

000019

Memorandum

Date: March 17, 2003

AD

From: Division of Food Contact Notifications, Chemistry Review Group 1

Subject: **FCN 314**: Hercules Inc. through Keller and Heckman. Use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard. Submissions dated December 18, 2002 (initial submission), February 7, 2003 (first response to deficiencies) and February 20, 2003 (second response to deficiencies).

To: Division of Food Contact Notifications, Regulatory Group 1
Attention: V. Gilliam

Keller and Heckman (K&H) on behalf of Hercules Inc. submitted this food contact notification (FCN) for use of the food contact substance (FCS) identified as 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard (internal sizing application). The FCS, identified as (b) (4) will be used at a level not to exceed 0.5% by weight of the dry paper and paperboard intended to contact all food types (I-IX), under conditions of use B-H, as described in Tables 1 and 2, respectively, of 21 CFR 176.170(c) (Components of paper and paperboard in contact with aqueous and fatty foods).

Background

The FCS was the subject of a prenotification consultation (PNC) meeting (PNC 114)[1] with Hercules Inc. on July 30, 2003. (b) (4) is not currently regulated in 21 CFR 170-199, nor is it the subject of any effective FCNs. The FCS and use limitations are similar to FCN 59[2] (effective 8/16/00) and FCN 255[3] (effective 9/5/02), submitted by Ciba Specialty Chemicals Corporation.

Identity and Manufacture

Information on the identity of the FCS is contained in FDA Form 3480, Part II Section A, and Attachments 1 and 2 of the initial submission.

CAS name: 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

[1] (b) (4)

[2] Chemistry memoranda for FCN 59 dated August 1, 2000 and August 10, 2000, R. Costantino to E. Machuga

[3] Chemistry memorandum for FCN 255 dated September 4, 2002; A. Bailey to H. Macon.

CAS Reg. No.: 464178-90-3

Other name: (b) (4)

Chemical Structure:

(b) (4)

Chemical/Physical information

Specifications were provided in Part II Section C of FDA Form 3480, and Attachment 4 of the notification. An aqueous solution of the polymer has a pH in the range of 3.5-6.3, and a viscosity in the range of 200-800 (cps, 22-23°C). The total solids weight % is in the range of 19-21%. The weight % polymer with a molecular weight below 1000 daltons is 3% (Attachment 7, Appendices D and E). A discussion on the low molecular weight portion of the FCS (i.e. with a molecular weight less than 1000 daltons) is provided in the Migration section below.

FCS characterization

Structural data identifying the FCS is included in Attachment 2 of the notification. The notifier provided proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra that are consistent with the structure of the subject FCS.

We have no questions on the identity of the FCS.

000732

Manufacture

Information concerning the manufacture of the FCS is described in FDA Form 3480, Part II Section B, and Attachment 3 of the notification. Raw material specifications are provided in Attachment 5.

Raw materials used in the manufacture of the FCS, as taken from Section II.B of the notification, are tabulated below.

Table 1: Raw Materials Used in the Manufacture of (b) (4)

Chemical	CAS No.	Function	Molar Ratios* (mole equivalents)
Mix of perfluoroalkyl iodides (PFAI)	25398-32-7	Starting material	1
(b) (4) (b)	(b) (4)	Starting material	1-2
Potassium hydroxide (PH)	1310-58-3	Reagent	1-1.25
Triethylenetetramine (TETA)	112-24-3	Starting material	0.4-1
Epichlorohydrin (ECH)	106-89-8	Starting material	0.5-2
(b) (4)			
Water	7732-18-5	Solvent	See below

* All mole equivalents and wt-% (in the case of water) are expressed relative to the moles or weight of PFAI.

(b) (4)

Impurities

Information on impurities in the FCS is contained in FDA Form 3480, Part II Section B.3, of the initial submission and the submissions dated February 7 and 20, 2003. Typical residual levels of each impurity are included in Section B.3; however, supporting data, such as analytical methods and

raw data including standard solutions and corresponding calibration curves, were only provided for ECH and [redacted] (Appendices B and C of Attachment 7). Since exposure (see below) to FTI, [redacted] FI, FE, ECH and [redacted] will be based on 100% migration to food and not on actual migration results, we requested (in e-mail messages dated January 24, 2003 and February 14, 2003) that the notifier provide analytical data to support the reported residual levels. In the submission dated February 20, 2003, the notifier provided the requested data (analytical methods and raw data including standard solutions and corresponding calibration curves) to demonstrate the residual levels of these 6 impurities in the FCS. Impurities and their residual levels (typical), as taken from Section B.3, and the February 20, 2003 submission, are tabulated below.

Table 2: Impurities in the FCS

[redacted]

The residual levels reported in Table 2 (above), as taken from the supporting analytical data [redacted]

We have no questions on the manufacture of the FCS.

Intended Use

Information concerning the intended use of the FCS is discussed in FDA Form 3480, Part II Section D.1-2, of the initial submission.

The notifier intends to use the FCS as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard (internal sizing application). The maximum use level of the FCS will not exceed 0.5% by weight of the dry paper and paperboard intended for use in contact with all food types (I-IX) under conditions of use B-H, as described in Tables 1 and 2 of 21 CFR 176.170(c), respectively.

The suggested notification language is provided in Attachment 9 and is consistent with the proposed use of the FCS.

We have no questions about the intended use of the FCS.

Technical Effect

Information on the technical effect of the FCS is contained in FDA Form 3480, Part II Section D.3, and Attachment 6 of the initial submission.

Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water. The notifier provided data illustrating the efficacy of the FCS as an oil/grease resistant sizing agent in Attachment 6 of the notification. Three different tests (kit test, pet food test and the Hercules size test) were conducted on treated paper (3 samples) and an untreated control. The results were then compared to leading commercial products in the market. A brief description of each test and a summary of the results follow.

Kit test

The kit test is an oil sizing test that consists of applying drops of 16 different mixtures of castor oil/heptane/toluene to the surface of paper. The drops are wiped off the paper after 15 minutes and the mixtures are ranked from least aggressive to most aggressive using a numbering system, with higher numbers corresponding to an increased sizing performance. If the paper is visually stained, it fails the test using that particular mixture.

Pet food test

The pet food test, an oil sizing test, involves the application of pet food to paper to determine the level of staining. The test consists of placing a metal ring containing ground pet food (minimum 23% chicken fat content) on top of a flat piece of paper to be tested. This is placed on top of a grid sheet that is placed on a flat aluminum metal plate. The stack of materials is heated at a constant temperature (60-90°C) for 2-24 hours, under pressure. At the end of this time period, the percent surface area of the grid sheet that has been stained is determined and recorded on a scale of 0-100%, with lower staining corresponding to better oil repellency. Commercially treated paper is typically considered to be <5% staining.

Hercules size test (HST)

HST, a well-recognized test for measuring sizing performance,[4] involves the application of dye to paper to determine the change in reflectance of the paper's surface. An aqueous solution of dye, such as napthol green dye in 1% formic acid, is contained in a ring on the top surface of the paper. The solution penetrates to the bottom surface, and the change in reflectance from the bottom surface is measured photoelectrically. This test is limited by choosing a convenient end point, *e.g.*, a reduction of 20% in reflected light corresponding to 80% reflectance. The time (in seconds) is recorded until the end point is reached, with longer times correlating to an increase in the resistance to water penetration. For example, unsized paper fails at zero seconds while moderately sized paper will register times from 21-150 sec.

Test results

The FCS,[5] when compared to other leading commercial products, performed exceptionally well. In the kit test, the FCS was comparable to other leading commercial products whereas in the pet food test and the Hercules size test, the FCS yielded better results, *i.e.* lower numbers in the pet food test and higher numbers in the HST, than those obtained with leading commercial products. An average use level of the FCS was reported to be in the range of 0.05-0.5%.

The notifier adequately demonstrated the technical effect of the FCS. We have no questions about the technical effect of the FCS.

Stability

Information on the stability of the FCS is provided in FDA Form 3480, Part II Section E, of the initial submission.

The FCS is reported to be stable under the intended use conditions of B-H (<100°C). Given that the FCS is a polymer, we concur.

We have no questions regarding the stability of the FCS.

Migration Studies

Migration results were reported in FDA Form 3480, Part II Section F.1, with the full report provided in Attachment 7 of the initial submission, and summarized below.

Test samples and Protocol

Migration studies were performed (in triplicate) on commercially prepared sheets (50 mg paper/in^2 basis weight). The sheets were either internally sized (to determine migration of (b) (4) and 3-CPD) or surface sized (to determine migration of (b) TETA and 3-perfluoro-n-octylprop-2-enol

[4] HST is described in Casey, J P., *Pulp and Paper Chemistry and Chemical Technology, Volume 3*, 1981, pp. 1553-1554

[5] FCS sample specifications: pH of 4 9, viscosity in the range of 290-400 (cps, 22-23°C), and an average total solids of 19.6 wt-%.

(FA; representing the C_6-C_{18} fluorinated alcohols)). Internally treated (containing 0.35 and 0.5% by weight of the FCS)[6] and untreated (control) sheets were immersed in 10% ethanol (as a non-fatty food simulant) and corn oil (as a fatty food simulant). Surface treated (containing 0.35 and 0.5% by weight of the FCS) and untreated sheets were immersed in 10% ethanol and either corn oil or 50% ethanol (as a fatty food simulant).

Treated and untreated (control) commercially prepared sheets (2.5" x 2.5" pieces, 20 pieces for each individual extraction, 120 in^2 total surface area exposed)[7] separated by screens, were placed in two-sided extraction cells (capable of withstanding high pressures) along with the food simulant (240 mL), giving a food simulant-to-surface area ratio of 2 mL/in^2 paper. The samples were extracted (in triplicate) for 2 hr at 100°C followed by 238 hr at 40°C. For surface treated samples, extracts were analyzed at 2 and 240 hr (a total of 6 extractions for each food simulant). For internally treated samples, extracts were analyzed after 2, 24, 96 and 240 hrs (a total of 12 extractions for each food simulant). Analytical methods used by the notifier are described in Appendices B and G of Attachment 7, and are summarized below.

Analysis

Sample extracts were analyzed by gas chromatography using electron capture detection (GC-ecd), high performance liquid chromatography (HPLC) with a fluorescence or XSD detector, or liquid chromatography with tandom mass spectrometry (LC/MS/MS). As noted above, the extracts were analyzed at 2, 24, 96 and 240 hrs for (b) (4) and 3-CPD (internally treated sheets), and at 2 and 240 hrs for (b) (4) FA and TETA (surface treated sheets).

(b) (4) *and 3-CPD*

Analytes were first separated from the aqueous extract through a liquid-liquid extraction column. (b) (4) and 3-CPD were then derivatized with heptafluorobutylimadazole (HFBI) and analyzed by GC-ecd.

Standard solutions of (b) (4) in 10% ethanol (0.000238, 0.000475, 0.001188, 0.002375, 0.00475 and 0.007125 µg/mL) and corn oil (0.001968, 0.003936, 0.007872, 0.015744 and 0.03936 µg/mL) were prepared by serial dilution of a stock solution of (b) (4) (b) (4) and 3-CPD in acetonitrile. Standard solutions of 3-CPD in 10% ethanol (0.000262, 0.000524, 0.00131, 0.00262, 0.00524 and 0.00786 µg/mL) and corn oil (0.002388, 0.004766, 0.009552, 0.019104 and 0.04776 µg/mL) were prepared by serial dilution of a stock solution of (b) (4) (b) (4) and 3-CPD in acetonitrile. The solutions were analyzed by GC-XSD. Calibration curves in 10% ethanol and corn oil were provided in Appendix F of Attachment 7 (pp. 129-130).

(b) (4)

Analytes were prepared by addition of potassium bromide, concentrated hydrobromic acid (to adjust the solution pH between 1 and 3), saturated bromine water, 1M sodium thiosulfate and sodium sulfate to sample extracts (or standards). The solutions were extracted and the organic layers were

[6] Corresponding to 7 and 10 lbs/ton, respectively.

[7] In the case of TETA: 20 2" x 2" square pieces separated by metal screens. Total food simulant 200 mL. Total surface of paper exposed 80 in^2.

passed through sodium sulfate. The solutions were then diluted with ethyl acetate and analyzed by GC-ecd.

Six standard solutions in 10% ethanol (0.0251, 0.075, 0.075, 0.0251, 0.075, and 0.251 µg/mL) were prepared by serial dilution of an (b) stock solution, and analyzed by GC-ecd. A calibration curve in 10% ethanol was provided in Appendix A of Attachment 7 (p. 15).

(b) (4)

TETA

Analytes were prepared by addition of 0.1 M NaOH and the derivatizing agent fluorescamine (solution in acetone) to the test solutions. 10% Ethanol samples were allowed to stand for approximately 2 hours for the derivatization to be complete, while 50% ethanol samples stood for approximately 12 hours.

Standard solutions (2.5, 5.0, 10, 25, 50 and 100 ng/mL) in 10% and 50% ethanol were prepared by serial dilution of a TETA stock solution in 50% ethanol. The solutions were analyzed by LC/MS/MS (Appendix G).[8] No calibration curves were provided by the notifier.

Additional Analytes

The notifier did not analyze the extracts for migration of FTI, FI, (b) (4) FE, ECH or (b) (4)

Migration Results

Internally Treated Paper

Test conditions and corresponding migration values (average for each time period) for internally treated sheets (containing 0.5 wt-% FCS), as taken from Form 3480 Section II.F, and Attachment 7[9] (Appendix F), are summarized below.

[8] In Attachment 7 (Appendix B p.44), the notifier discusses the analytical method for the determination for TETA in 10% and 50% ethanol. In Appendix G of Attachment 7, the notifier provides the full analytical report (including the analytical method) for the migration of TETA in 10% and 50% ethanol. We believe that the information provided in Appendix B is in error.

[9] The notifier erroneously reported migration results for (b) (4) and 3-CPD in Attachment 7 Section III.a

Table 3: Average Migration Results for Internally Treated Sheets (0.5 wt-% FCS)*

Food Simulant	Time/Temp Conditions	(b) (4) (µg/kg)	3-CPD (µg/kg)
10% Ethanol	2 hr/100°C	0.02	0.1
	24 hr/40°C	0.03	0.2
	96 hr/40°C	**0.03**	0.2
	240 hr/40°C	0.02	**0.2**
Corn Oil	2 hr/100°C	<0.04	0.04
	24 hr/40°C	<0.04	0.01
	96 hr/40°C	<0.04	0.07
	240 hr/40°C	**<0.04**	**0.2**

* Migrant concentrations assume 10 g of food/in^2 of paper. For exposure calculations, we will use migration results for testing conditions of 240 hr/40°C (see highlighted entries with the exception of 1,3-DCP in 10% ethanol).

Surface Treated Paper

Likewise, test conditions and corresponding migration values (average for each time period) for surface treated sheets (containing 0.35 and 0.5 wt-% FCS), as taken from Form 3480 Section II.F, and Attachment 7 (Section III.a and Appendices A ((b) FA) and G (TETA)), are summarized below. Migration results are based on non-detect levels using limits of detection (LODs) corresponding to 5, 10 and 1 µg/kg for (b) FA and TETA, respectively. Similar migration results were obtained for (b) and TETA with 0.35 and 0.5 wt-% of the FCS. In the case of FA, results were based on 0.5 wt-% of the FCS.

Table 4: Average Migration Results for Surface Treated Sheets (0.35 and 0.5 wt-% FCS)[a]

Food Simulant	Time/Temp Conditions	(b) (µg/kg)	FA (µg/kg)	TETA (µg/kg)
10% Ethanol	2 hr/100°C	<5	0.2	<1
	240 hr/40°C	**<5**	**0.2**	**<1**
Corn Oil	2 hr/100°C	---	**0.9**	<1[c]
	240 hr/40°C	---	0.7	**<1**[c]

[a] Migrant concentrations assume 10 g of food/in^2 of paper. For exposure calculations, we will use migration results for testing conditions of 240 hr/40°C (see highlighted entries with the exception of FA in corn oil).

[b] 50% Ethanol (as the fatty food simulant) was substituted for corn oil in the analysis of TETA.

The notifier provided migration results for (b) in 10% ethanol. Data in corn oil was not provided due to difficulties in the analysis of (b) in corn oil. The notifier claims that since the solubility of (b) in 10% ethanol is significantly higher than that of corn oil, a worse-case migration in a fatty food simulant could be represented by the 10% ethanol solvent. We concur with the notifiers claim.

Raw data, sample chromatograms and calibration curves supporting all the reported migration results, were provided in Attachment 7 of the initial submission and the February 20, 2003 submission.

Low-Molecular-Weight (LMW) Oligomers Containing TETA

The notifier did not analyze the test extracts described above for LMW oligomers. Rather, migration of LMW oligomers, *i.e.* the fraction having a molecular weight lower than 1000 daltons, was based on the wt-% present in the FCS and the assumption of 100% migration to food (see below).

Size exclusion chromatography (SEC) showed that 3% of the dry weight of the FCS consisted of LMW oligomers. The LMW oligomer fraction was further analyzed by 1D and 2D NMR experiments, such as COSY (correlated spectroscopy), HMQC (heteronuclear multiple quantum coherence) and HMBC (heteronuclear multiple bond coherence), to determine the proportion of TETA-related compounds. The level of LMW oligomers containing TETA was found to be 13,800 µg/g LMW oligomer (ppm based on the total solids weight) using equation 2 in Appendix E. Therefore, the LMW fraction composed solely of TETA-containing oligomers is 410 µg/g FCS (3% x 13,800 µg/g). A description of the analytical methods and corresponding spectra were provided in Appendices D and E of Attachment 7).

In the approach described above, the notifier determined that ~1.4% of the LMW fraction (3%) is composed of TETA-containing oligomers. While this may seem to be an artificially low level, we believe that the remaining fraction of LMW oligomers would contain fluorinated species. Exposure to the fluorinated containing-LMW oligomers would be accounted for in the exposure estimates to other fluorinated impurities, such as FTI, FI, FE and FA, determined below.

Validation

1,3-DCP and 3-CPD

Spiking and recovery studies were conducted (in triplicate) on the 10 day test extracts prior to sample work-up. Throughout the notification, the notifier reports that samples were spiked at ½, 1 and 2 times the detected levels in each food simulant. This is only true in 10% ethanol. Spiking levels in corn oil were at 5 and 1 times the detected level for (b) (4) and 3-CPD, respectively. Raw data, representative chromatograms and calibration curves were provided in Appendix F.

Average recoveries for (b) (4) were 35 ± 6 in 10% ethanol (p. 107) and 77 ± 9 in corn oil (p. 126). The recovery in 10% ethanol is lower than the limits for proper validation. However, this recovery is acceptable since (b) (4) hydrolyzes to 3-CPD during sample work-up, resulting in more dilute samples. Average recoveries for 3-CPD were 90 ± 12 (p. 107) and 78 ± 8 (p. 127) in 10% ethanol and corn oil, respectively.

(b) *TETA, and FA*

Spiking and recovery studies were conducted (in triplicate) on the 10 day test extracts prior to sample work-up. Samples were spiked at the LODs in each food simulant. Raw data, representative chromatograms and calibration curves were provided in Appendix A for (b) and FA, and in Appendix G for TETA.

No recoveries were reported for AA in 10% ethanol. Since the peak areas in the chromatograms of the samples spiked at the LOD (Appendix A pp. 23-24) appear larger than those of the migration samples (Appendix A pp. 20-21), we will consider the method appropriately validated.

Average recoveries for TETA were 102 ± 24 and 102 ± 15 in 10% and 50% ethanol, respectively (Appendix G of Attachment 7). Average recoveries for FA were 170 ± 8 in 10% ethanol, and 24 ± 1 in corn oil. These recoveries are higher (10% ethanol) and lower (corn oil) than what we typically accept. We believe that these values reflect the difficulties in working with a polar alcohol such as FA. We will therefore use the migration values (based on the LOD) without any correction factor, making our exposure estimates for FA conservative.

We have no questions about the migration and validation studies performed on the FCS.

Consumer Exposure

Exposure estimates can be found in FDA Form 3480, Part II Section F, of the initial submission. The exposure estimates for low-molecular-weight (LMW) oligomers containing TETA and impurities in the FCS were determined using actual migration results or the assumption of 100% migration to food. The exposure estimates are presented below.

Low-molecular-weight (LMW) oligomers containing TETA

The notifier did not perform migration studies on the LMW oligomers. Instead, the notifier calculated the dietary concentration (DC) of LMW oligomers containing TETA using the previously discussed SEC data and the assumption of 100% migration to food. The notifier calculated exposure to LMW oligomers based on the following assumptions:

1. 100% migration of the LMW oligomers to food.
2. LMW oligomers having a molecular weight <1000 dalton and containing TETA, are present in the FCS at a level of 410 mg oligomer/kg FCS.
3. The maximum level of the FCS in paper is 0.5 g FCS/100 g paper.
4. A paper basis weight of 50 mg paper/in^2 paper.[10]
5. A food mass-to-surface area ratio of 10 g food/in^2 paper.

The concentration of the TETA-containing LMW oligomers in food (<M>) was calculated as follows:

$$\left(\frac{410x10^{-6}\ g\ oligomers}{g\ FCS}\right)\left(\frac{0.5\ g\ FCS}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{in^2\ paper}\right)\left(\frac{in^2\ paper}{10\ g\ food}\right)=10x10^{-9}\frac{g\ oligomer}{g\ food}=10\ ppb$$

Using the <M> (calculated above) and a consumption factor (CF) of 0.05 for specialty treated paper,[11] the DC of the FCS is:

[10] In a memorandum of meeting dated April 13, 1995 written by A Bailey, it was determined that the average basis weight of paper for these types of calculations would be 50 mg/in^2. This conclusion was supported by the observation that food-contact paper and paperboard basis weights range from 20-100 mg/in^2.

[11] A CF of 0.05 is representative of specialty paper See the chemistry memorandum for FCN 255 dated September 4,

DC_{FCS} = CF x <M> = 0.05 x 10 ppb = 0.5 µg/kg or 0.5 ppb

The estimated daily intake (EDI), based on a daily diet of 3 kg food/person/day, is:

EDI_{FCS} = 3 kg food/p/d x 0.5 µg FCS/kg food = 1.5 µg FCS/p/d

We concur with the notifiers exposure estimates for the FCS (as TETA containing-LMW oligomers).

Residual Impurities

(b) (4) *3-CPD, TETA and FA*

We calculated exposure to these impurities based on the notifier's reported migration results (Tables 3 and 4 above),[12] the paper and paperboard food-type distribution factors ($f_{aqueous + acidic} = 0.59$, $f_{alcohol + fatty} = 0.41$), and a CF of 0.05. The DC and EDI of (b) (4) is calculated below:

$DC_{1,3\text{-DCP}} = CF \times [(f_{aqueous + acidic} \times M_{10\% \text{ Ethanol}}) + (f_{alcohol + fatty} \times M_{Corn\ oil})]$

= 0.05 [(0.59 x 0.02 ppb) + (0.41 x <0.04 ppb)] = <1.4 ng/kg or <1.4 pptr

$EDI_{1,3\text{-DCP}}$ = <1.4 ng (b) (4) kg food x 3 kg food/p/d = <4.2 ng (b) (4) p/d

Similarly, the DCs and EDIs for 3-CPD, TETA and FA were calculated and tabulated below.

Table 5: Exposure Estimates Based on Actual Migration Results

Impurity	Migration[a] (µg/kg or ppb)	DC (ng/kg or pptr)	EDI (ng/p/d)
(b) (4)	0.02 (10% ethanol) <0.04 (corn oil)	<1.4	<4.2
3-CPD	0.2 (10% ethanol) 0.2 (corn oil)	10	30
TETA[b]	<0.5 (10% ethanol) <0.5 (50% ethanol)	<25	<75
FA[c]	0.2 (10% ethanol) 0.7 (corn oil)	40	120

[a] From Tables 3 and 4, above.

[b] ½ the LOD was used in exposure calculations based on the non-detection of TETA.

2002 (effective September 5, 2002; A. Bailey to H. Macon) and the chemistry memorandum for FCN 59 dated August 1, 2000 (effective August 16, 2000, R. Costantino to E. Machuga).

[12] Since the FCS is intended to be applied internally, both the internal and external migration results can be used to conservatively estimate exposures

[c] <M> was multiplied by a factor of 2 to account for all congeners.

The DCs reported by the notifier for [redacted] and 3-CPD are similar to those values we report in this memorandum. However, those values reported by the notifier for TETA and FA are ~50 times lower than the values we report in the table above. The notifier assumed that 2% of the non-substantive material remains with the finished paper, an assumption that is not appropriate when calculating exposure based on actual migration results.

[redacted] FTI, FI, FE, ECH, [redacted]

The notifier did not analyze the test extracts for these impurities, with the exception of [redacted][13] Nonetheless, the notifier reported DCs for FTI, FI, FE, ECH and [redacted] using the reported residual levels and assuming 100% migration to food.

We employ a different approach to model the internal addition of a non-substantive paper additive to paper. This is referred to as our "wet-end" model[14] in the FCN/FAP guidance document. This model is also acceptable for water-soluble impurities in a FCS. While the impurities [redacted] FTI, FI, FE, ECH and [redacted] may not necessarily have a high water solubility, we would expect them to have significant water solubility given their low residual levels in the FCS (see Table 1, above). The following assumptions are made in our "wet-end" model:

1. The substance is not substantive to paper.
2. Additives are typically introduced into the papermaking process at the headbox,[15,16] which contains a whitewater slurry consisting of about 0.6 weight % pulp.[17,18]
3. Prior to entering the dryers, the whitewater slurry (containing the additive) is concentrated to contain approximately 33% pulp and 67% water. Since the additive is not substantive to paper, the mass of water (containing the additive) in contact with pulp at the point in the papermaking process where the slurry enters the dryers, determines the level of additive retained in the paper.
4. Any substance present after sheet forming remains in the finished paper on steam drying.

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[13] The notifier provided migration results (based on the LOD) for [redacted] in 10% ethanol. The exposure we calculated for [redacted] based on actual migration results was ~20 times higher than the exposure to [redacted] based on 100% migration to food. Therefore, we will report exposure to [redacted] based on the assumption of 100% migration to food.

[14] For a more detailed description of the "wet end" model see the chemistry memorandum for FAP 5B4472 dated April 16, 1996, A Bailey to D. Harrison, and the chemistry memorandum for FAP 3B4367 dated April 30, 1999, A Bailey to V. Gilliam

[15] Casey, J.P., *Pulp and Paper Chemistry and Technology, Volume 2: Papermaking*, 2nd ed., New York Interscience Publishers, Inc , 1960, pp. 947 and 1013-1014.

[16] The headbox is a pressurized flowbox that distributes paper stock onto the Fourdrinier wire, an endless screen belt that enhances drainage, as the paper sheets are formed. See Smook, G , *Handbook for Pulp and Paper Technologists*, Joint Executive Committee of the Vocational Education Committee of the Pulp and Paper Industry, 1992, p.208

[17] See, for example, Calkin, J.B. and J.L. Parsons in *Modern Pulp and Paper Making*, ed J.B. Calkin, 3rd ed , New York: Reinhold, 1957, Ch. 11, p. 312

[18] White water is a general term for water removed from a pulp slurry and containing fiber fines and additives On the paper machine, white water is the water that flows through the Fourdrinier as the paper sheets are formed White water is frequently recycled in the papermaking process. The terms "white water" and "process water" are interchangeable. See Smook, G , *Handbook for Pulp and Paper Technologists*, Joint Executive Committee of the Vocational Education Committee of the Pulp and Paper Industry, 1992, pp. 227, 395.

5. Finished paper contains approximately 92% pulp and 8% water.
6. The basis weight of paper is 50 mg/in^2.[10]
7. 100% migration of the FCS from the finished paper to food.
8. A food mass-to-surface area ratio of 10 g food/in^2 paper.
9. A CF of 0.05.

As an example, the DC of (b) is calculated below. The residual level (typical) of (b) in the FCS (see Table 2, above) is 484 mg/kg, and the FCS is added at the "wet end" at a maximum of 0.5% by weight/g paper. The (b) in the water slurry is found to be:

$$\left(\frac{484x10^{-6}\ g\ AA}{g\ FCS}\right)\left(\frac{0.5\ g\ FCS}{100\ g\ paper}\right)\left(\frac{100\ g\ paper}{92\ g\ fiber}\right)\left(\frac{0.6\ g\ fiber}{100\ g\ slurry}\right)=1.6x10^{-8}\ g\ (b)\ /\ g\ slurry$$

The concentration of (b) in the finished paper is then calculated.

$$\left(\frac{1.6x10^{-8}\ g\ AA}{g\ slurry}\right)\left(\frac{67\ g\ slurry}{33\ g\ fiber}\right)\left(\frac{92\ g\ fiber}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{in^2\ paper}\right)\left(\frac{in^2\ paper}{10\ g\ food}\right)=0.15x10^{-9}\ g\ (b)\ g\ food$$

The DC and EDI of (b) from the proposed use of the FCS is:

(b) (4) = CF x <M> = 0.05 x 0.15 µg (b) (4) food = 7 ng/kg or 7 pptr

(b) (4) = 21 ng/p/d

Similarly, exposures to FTI, FI, FE, ECH and (b) (4) were calculated and tabulated below.

Table 6: Exposure Estimates Based on our "Wet-End" Model

Substance	Typical residual* (dry basis, mg/kg)	<M> (ng/kg or pptr)	DC wet-end model (ng/kg or pptr)	EDI (ng/p/d)
(b)	484	0.15 µg/kg	7	21
FTI	<178 (total)	<54	<2.7	<8
FI	<74 (total)	<22	<1.1	<3.3
FE	<71 (total)	<21	<1	<3
ECH	2.3	0.7	0.04	0.1
(b) (4)	8.2	2.5	0.1	0.3

* From Table 2, above.

(b) (4)
The DC of TMSN using our "wet-end" model and a residual level of 171 mg/kg (see Table 2, above) was determined to be 2.6 ng/kg (or pptr), corresponding to an EDI of 7.8 ng/p/d. We note that AIBN is cleared in 21 CFR 176.170 for use in the manufacture of paper and paperboard.

Risk Assessments

Upper-bound risk estimates for ECH, (b) (4) 3-CPD and (b) (4) were calculated by the notifier. We recalculated upper bound risks for the 4 impurities by multiplying our EDI (in mg/kg-bw/d) by the carcinogenic unit risk [in $(mg/kg\text{-}bw/d)^{-1}$]. The results are tabulated below.

Table 7: Upper-Bound Risk Estimates

Substance	Unit risk* $(mg/kg\text{-}bw/d)^{-1}$	EDI (mg/kg-bw/d)	Upper-bound unit risk
ECH	0.0027	$2x10^{-9}$	$5.4x10^{-12}$
2,3-DCP	0.034	$5x10^{-9}$	$1.7x10^{-10}$
3-CPD	0.0109	$5x10^{-7}$	$5.5x10^{-9}$
(b) (4)	0.034	$7x10^{-8}$	$2.4x10^{-9}$

* Unit risk values as found in our database (ECH) or in the February 10, 2000 memorandum from the Division of Heath and Human Effects Evaluation ((b) (4) 3-CPD and (b) (4)

Notification Language

The acknowledgment letter, as signed off by Chemistry on March 4, 2003, is appropriate as written. The language in the acknowledgement letter differs slightly from the suggested language provided by the notifier in Attachment 9.

Conclusion

We have no questions on this FCN.

(b) (4)

Sharon Elyashiv-Barad, Ph.D.

(b) (4)

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Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

e Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2. CAS Registry Number

464178-90-3

3. Trade or Common Name

4. Other Chemical Names (IUPAC, etc.)

n/a

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

See FCN No. 314, Attachment 1 for chemical structure. The chemical formula is:

$H\text{-}(C_2H_5N)_{x1}\text{-}(C_5H_{11}NO_2)_{x2}\text{-}(C_5H_{10}NOCl)_{x3}\text{-}(C_5H_9NOCl)_{x4}\text{-}(C_5H_{10}NON\text{-x link})_{x5}\text{-}(C_{11\text{-}23}H_{10}NOF_{13\text{-}37})_{x6}\text{-}(C_8H_{17}NO_3Cl)_{x7}\text{ -}C_{12\text{-}24}H_{12}N\text{-x link}F_{13\text{-}37}$

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Mw = 3,067,499 Daltons
Mn = 24,368 Daltons

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

^{13}C NMR and ^{1}H NMR spectra are included in FCN No. 314, Attachment 2.

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Section B - MANUFACTURE

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e Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
Mix of perfluoralkyl iodides	25398-32-7	Starting material
Triethylenetetramine	112-24-3	Starting material
Epichlorohydrin	106-89-8	Starting material

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See Attachment 1 for manufacturing information.

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Section B - MANUFACTURE - Continued

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9. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
Flourinated telomer iodide starting material	25398-32-7	<184 ppm (total) **	
		<37 ppm	
		<61 ppm (total) **	
		171 ppm	
		<61 ppm (total) **	
		2989 ppm	
Epichlorohydrin	106-89-8	2.3 ppm	
2,3-Dichloro-1-propanol (2,3-DCP)	616-23-9	8.2 ppm	
1,3-Dichloro-1-propanol (1,3-DCP)	96-23-1	58 ppm	
3-Chloro-1,2-propanediol (3-CPD)	96-24-2	84 ppm	
Triethylenetetramine (TETA)	112-24-3	unknown	
		55 ppm	

** As described on page 116 of the migration report in FCN No. 314, Attachment 7, each of these impurities is made up of a range of congeners. In each case, the C_8 is the most abundant, constituting one-half or more of the various congeners. Therefore, if the C_8 is not detected in residual analyses, the other congeners will also not be detected. For this reason, the C_{10} and C_{12} congeners were not necessarily included on the chromatograms provided. Nonetheless, rather than taking one-half of the detection limit for each species in our 100% migration calculations, we are using the detection limit amount so as to include all the congeners.

nsure that exposures to these substances are addressed in Section II.G of this form.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
e Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

Property	Max. Value	Min. Value	Individual Batch Values

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Test methods are provided in FCN No. 314, Attachment 4.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Weight percent polymer below 1000 Daltons = 3%
Weight percent polymer below 500 Daltons is not available

(See FCN No. 314, Attachment 7; pp. 9, 128-140)

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil/grease resistant sizing agent in the manufacture of paper and paperboard at levels up to 0.5% by weight of the dry paper and paperboard intended for use in contact with food. Single use of the food-contact material is anticipated.

a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
FCS in paper and paperboard up to 0.5% by weight of the dry paper and paperboard	All food types (Types I – IX)	B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

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Part II — CHEMISTRY INFORMATION - CONTINUED

State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil/grease/fat and water stains can weaken paper, making it susceptible to punctures and tears. In addition, the stains hurt the print quality of the paper and can make the bag appearance undesirable to the consumer. When the oil/grease/fat or water contained in the paper bag/container wets the outer surface of the bag/container, the surfaces the paper comes in contact with can become slippery, creating a safety hazard. Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water.

Data demonstrating the technical effect of the FCS are provided in FCN No. 314, Attachment 6. Three different types of tests were conducted (Kit number, Pet Food Test, and HST), comparing the FCS to four of the leading commercial products in the market. Three batches of the FCS, as well as an untreated paper control, were compared to these commercial products.

The minimum amount needed to achieve the intended technical effect is 0.05% - 0.5%.

Section E - STABILITY DATA

See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

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Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option

See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

The test specimens used in the migration study consisted of commercially prepared sheets weighing 50 lbs/3000 ft^2. This is equivalent to 52.4 mg paper/in^2 (50 lbs x 453 g/lb x 1000 mg/g ÷ 3000 ft^2 ÷ 144 in^2/ft^2 = 52.4 mg/in^2). Untreated sheets were used as controls, and treated sheets were prepared containing 0.5% by weight of the FCS. The FCS was applied to the samples as a surface treatment. The FCS used to prepare the treated sheets contained the impurities and their respective concentrations found in Part II, Item 1 of this FCN (page 5). The residual levels of these impurities were not determined in the treated test specimens. The treated test specimens and control specimens were immersed in the food simulating solvents.

A copy of the migration study report is included in Attachment 2.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

The aqueous food simulant (10% ethanol) and fatty food simulant (corn oil) were exposed to both sides of the sample and control sheets at a volume-to-surface area ratio of 2 mls/in^2 (1-side area). No turbidity or precipitation was observed in the sample extracts. Aliquots of the control and sample extracts were analyzed at 2 and 240 hours for 1,3-DCP and 3-CPD. The 24 and 96 hour extracts were not analyzed since either the initial 2 hour migration level was higher than the 240 hour migration level or there were no differences.

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Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in² 0.011 mg/in² 0.021 mg/in²	0.015 mg/in²
			40°C analysis after 24 hours	0.015 mg/in² 0.014 mg/in² 0.022 mg/in²	0.017 mg/in²
			40°C analysis after 96 hours	0.017 mg/in² 0.017 mg/in² 0.023 mg/in²	0.019 mg/in²
			40°C analysis after 240 hours	0.020 mg/in² 0.021 mg/in² 0.023 mg/in²	0.021 mg/in²

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food/Food Simulant	Temp/time of analysis	Migration ($\mu g/in^2$)			Avg. ($\mu g/in^2$) Migration
50 lb/3000 ft^2 uncoated paper sheets treated at 0.6% dry weight FCS	1,3-DCP	10% ethanol	100° C; analysis after 2 hours	< 0.0010	< 0.0010	< 0.0010	< 0.0010
			40° C; analysis after 240 hours	< 0.0010	< 0.0010	< 0.0010	< 0.0010
		Corn oil	100° C; analysis after 2 hours	0.001006	0.001535	0.001111	0.0012
			40° C; analysis after 240 hours	0.000967	0.001067	0.000932	0.0010
	3-CPD	10% ethanol	100° C; analysis after 2 hours	< 0.0010	< 0.0010	< 0.0010	< 0.0010
			40° C; analysis after 240 hours	< 0.0010	< 0.0010	< 0.0010	< 0.0010
		Corn oil	100° C; analysis after 2 hours	0.017458	0.022658	0.020664	0.020*
			40° C; analysis after 240 hours	0.0149399	0.0149142	0.0133165	0.013*

* Corrected for control

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Migration of the following analytes is addressed in FCN No. 314: Allyl alcohol, [redacted] and TETA

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Analyte	10% Ethanol			Corn oil		
	Amount added (ug/in^2)	% Recovery	% RSD	Amount added (ug/in^2)	% Recovery	% RSD
1,3-DCP	0.0010	68.0	12	0.0010	78.7	5.7
3-CPD	0.0010	78.0	1.3	0.0010	81.7	8.3

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

The following calculations utilize the residual levels provided in Part II, B, 3, and assume (1) 50 mg paper/in^2 treated with 0.5% FCS, and (2) 100% migration to 10 g food/in^2.

FCS

See FCN No. 314, Attachment 7, p. 9 for explanation of maximum oligomer residual level.
50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000410 mg oligomers/mg FCS ÷ 10,000 mg food/in^2 = 1.03 x 10^{-8} mg oligomers/mg food = 10.3 ppb

IMPURITIES

Data that support the residual levels of these impurities in the FCS were provided in FCN No. 314, Attachment 7, and in a February 20, 2003 letter supplementing that FCN.

50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.0000023 mg epichlorohydrin/mg FCS ÷ 10,000 mg food/in^2 = 5.75 x 10^{-11} mg epi/mg food = 0.06 ppb

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50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.0000082 mg 2,3-DCP/mg FCS ÷ 10,000 mg food/in^2 = 2.05 x 10^{-10} mg 2,3-DCP/mg food = 0.2 ppb

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50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000184 mg [redacted] /mg FCS ÷ 10,000 mg food/in^2 = 4.6 x 10^{-9} mg [redacted] /mg food = 4.6 ppb

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50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000061 mg [redacted] /mg FCS ÷ 10,000 mg food/in^2 = 1.5 x 10^{-9} mg [redacted] /mg food = 1.5 ppb

50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000061 mg [redacted] mg FCS ÷ 10,000 mg food/in^2 = 1.5 x 10^{-9} mg [redacted] /mg food = 1.5 ppb

000018

As explained on page 5 above, the fluorinated impurities are comprised of a range of congeners, with C_8 being the most abundant at approximately 50%. Thus, to be conservative, we have doubled the 55 ppm [redacted] residual level to account for all of the congeners:

50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.00011 mg [redacted] /mg FCS ÷ 10,000 mg food/in^2 = 2.75 x 10^{-9} mg [redacted] /mg food = 2.75 ppb

Section G- ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

One-half the sensitivity level is used below as the maximum level of migration where a substance was not detected at a given sensitivity, and where the chromatography supports the use of one-half the detection limit. In addition, all migration values in µg/in^2 were converted to µg/kg food (ppb) as follows: µg/in^2 ÷ 0.01 kg food/in^2 = µg/kg. A consumption factor (CF) of 5% for specialty paper and the food type distribution factors for uncoated paper (59% aqueous, 41% fatty) are used below to calculate the EDI for each substance.

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(Migration data for TETA, [redacted] and the [redacted] were included in FCN No. 314.)

TETA = 0.05 CF x 0.5 µg/kg = 0.025 µg/kg (ppb) x 3 kg/p/d = 0.075 µg/p/d
= 0.05 CF x 2.5 µg/kg = 0.125 µg/kg (ppb) x 3 kg/p/d = 0.375 µg/p/d

[redacted] CONFIDENTIAL

[redacted] = 0.05 CF x 2 x [(0.59) (0.19 µg/kg) + (0.41)(0.94 µg/kg)] = 0.05 µg/kg (ppb) x 3 kg/p/d = 0.15 µg/p/d

1,3-DCP = 0.05 CF x [(0.59) (0.05 µg/kg) + (0.41)(0.12 µg/kg)] = 0.0039 µg/kg (ppb) x 3 kg/p/d = 0.012 µg/p/d
3-CPD = 0.05 CF x [(0.59) (0.05 µg/kg) + (0.41)(2 µg/kg)] = 0.042 µg/kg (ppb) x 3 kg/p/d = 0.13 µg/p/d

We note that the migration results for 1,3-DCP and 3-CPD are conservative, as the use level in preparing the test samples was 0.6%, rather than the lower 0.5% use level requested in this FCN.

The remaining dietary exposure calculations are based on 100% migration calculations provided in Section F(2).

Oligomers = 0.05 CF x 10.3 ppb = 0.515 ppb (µg/kg) x 3 kg/p/d = 1.55 µg/p/d
Epichlorohydrin = 0.05 CF x 0.06 ppb = 0.003 ppb (µg/kg) x 3 kg/p/d = 0.009 µg/p/d CONFIDENTIAL
2,3-DCP = 0.05 CF x 0.2 ppb = 0.01 ppb (µg/kg) x 3 kg/p/d = 0.03 µg/p/d

[redacted]
= 0.05 CF x 4.6 ppb = 0.23 ppb (µg/kg) x 3 kg/p/d = 0.69 µg/p/d
= 0.05 CF x 1.5 ppb = 0.075 ppb (µg/kg) x 3 kg/p/d = 0.225 µg/p/d
= 0.05 CF x 1.5 ppb = 0.075 ppb (µg/kg) x 3 kg/p/d = 0.225 µg/p/d CONFIDENTIAL
= 0.05 CF x 2.75 ppb = 0.138 ppb (µg/kg) x 3 kg/p/d = 0.413 µg/p/d

[redacted]

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in tion II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

000019

Memorandum

Date: April 26, 2005

From: Division of Food Contact Notifications
Chemistry Review Group II

Subject: FCN 487: Hercules Inc., through Keller and Heckman, L.L.P., submissions dated 12/16/04, 2/14/05, and 3/16/05 for the use of a perfluorinated oil/grease-resistant sizing agent for food contact paper and paperboard

To: Division of Food Contact Notifications
Regulatory Group II
Attn: P. Honigfort, Ph.D

Hercules Inc., through Keller and Heckman, L.L.P., submitted this food contact notification for the use of a perfluorinated oil/grease-resistant sizing agent for food contact paper and paperboard. The notification outlines a new synthetic method for this food contact substance (FCS) and identifies new impurities and new residual levels for previously know impurities in this FCS. The notifier also requests the use of the FCS be expanded to include size press applications. The use level for the FCS is identical to that described in FCN 314, 0.5% by weight of the dry paper and paperboard.

Regulatory Status

The FCS is not currently regulated in 21 CFR 170-199 but it is the subject of one effective FCN (FCN 314), which is incorporated by reference. The FCS is similar to the FCSs described in FCN 59[1] (effective 8/16/00) and FCN 255[2] (effective 9/5/02), submitted by Ciba Specialty Chemicals Corporation. The notifier also submitted . The notifier has incorporated by reference the perfluorooctanoic acid analysis provided in .

Identity

Information on the identity of the FCS is contained in FDA Form 3480, Part II Section A of FCN 487 and in Attachments 1 and 2 of FCN 314.[3]

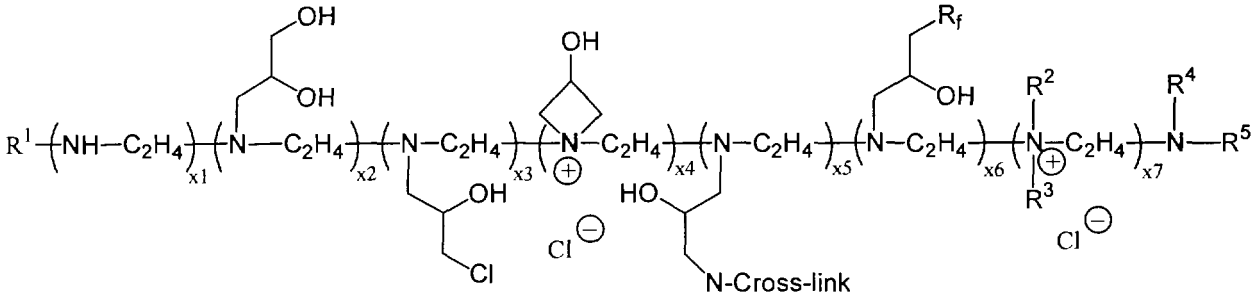
CAS Name: 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

[1] Chemistry memoranda for FCN 59 dated August 1, 2000 and August 10, 2000; R. Costantino to E. Machuga.
[2] Chemistry memorandum for FCN 255 dated September 4, 2002; A. Bailey to H. Macon.
[3] This information was reviewed in the chemistry memorandum dated 3/17/03 from S. Elyashiv-Barad to V. Gilliam on FCN 314.

CAS Reg. No.: 464178-90-3

Other name:

Chemical Structure:



R^1-R^5 = H, $CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2Cl$, $CH_2CH(OH)CH_2$(N-Cross-link), $CH_2CH(OH)CH_2R_f$

R_f = $F(CF_2)_{6-18}$

X_1-X_7 can be in any order.
Molar ratios of X1:(X2+X3):X4:(X5+X7):X6 =

Molecular weight: M_n = 188,359 Daltons
M_w = 3,067,499 Daltons

The notifier referenced molecular weight data in FCN 314 to support the identity of their material. During our preliminary review of the notification, we noted a significant change in the manufacturing process from that described in FCN 314. Because of the changes in the manufacturing process, we requested the notifier provide new molecular weight data on the FCS. The notifier provided the requested calibration curves and representative chromatograms for the molecular weight determinations in the 2/14/05 update. Although the notifier indicates that there are no significant changes to the low molecular weight fraction of the current FCS when compared to that reported in FCN 314, we note that the number-average molecular weight of the FCS manufactured by the new method has increase substantially from 24,368 Daltons to 188,359 Daltons. We believe the significant increase in the number-average molecular weight is due to the way the

The weight average molecular weight of the FCS has remained at approximately 3 million Daltons.

A comparison of the molecular weight data provided in the 2/14/05 update with the data provided in FCN 314 reveals that the quantity of oligomers below 1000 Daltons has actually decreased. Therefore, the notifier has argued that the exposure to the oligomers would be no greater than that calculated in FCN 314. This decrease in low-molecular weight oligomers is what we would expect to see with a large increase in the number-average molecular weight. We agree with the notifier's conclusion that exposure to oligomers from the use of the FCS would be no greater than that calculated in FCN 314.

We also noted in our deficiency letter to the notifier that the changes in the manufacturing process could alter the impurity levels, and thus, the migration levels of these impurities. Therefore, we requested the notifier provide either new migration data for these impurities from the FCS prepared by the current manufacturing method or provide supporting data for their residual amounts in the FCS so that we can estimate exposure to these materials. The notifier responded to our request in the 2/14/05 update and argued that the manufacturing process had not significantly changed the product or its impurity profile and the new process involved [redacted] Therefore, the analytical analyses provided in FCN 314 were applicable to the product under review and their results would represent a worst-case scenario when estimating exposure to these impurities.

We reviewed the manufacturing process and the impurity levels provided in FCN 314 and FCN 487. We note that the impurity levels of the FCS produced by the method described in FCN 487 either have remained substantially the same or have been reduced. As with the oligomers, we believe that addition of [redacted] serves to increase the efficiency of the reaction, decreasing the amount of byproducts formed during production of the FCS.[4] Therefore, we agree with the notifier that the supporting data provided in FCN 314 for the analysis of impurities in the FCS are applicable to the current FCN.

Characterization

The notifier provided carbon-13 and proton NMR spectra for the FCS in Attachment 2 of FCN 314.[3] Although the number-average molecular weight of the FCS has increased, the spectroscopic features identified in the NMR spectra would not be expected to change significantly. Therefore, the data provided in FCN 314 are applicable to the material identified in this notification. The spectra are consistent with the proposed structure of the FCS.

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4 In the original manufacturing process, [redacted] serves to increase the number-average molecular weight, thus reducing the amount of low weight oligomers and some impurities in the finished resin. In addition, the manufacturing process outlined in FCN 314 did not contain a [redacted] The residual levels of 1,3-dichloropropanol and 3-chloropropane diol have been reduced significantly compared to those listed in FCN 314.

Manufacture

The notifier provided manufacturing information in Part II section B of Form 3480 and in Attachment 1 of FCN 487. The specifications for the raw materials are in Attachment 5 of FCN 314.

Impurities

Information on impurities in the FCS is contained in FDA Form 3480, Part II Section B.3, of FCN 487. Table 1 summarizes the typical residual levels of the impurities identified in the FCS as described in FCN 487 and FCN 314.

5 Therefore, exposure to these compounds will be essentially zero.

Table 1: Impurities in the FCS

Impurity	Function	CAS Reg. #	Typical residual (dry basis, mg/kg)	Typical residuals from FCN 314 (dry basis, mg/kg)
C_6-C_{18} Fluorinated telomer iodides (PFAI)	Starting material	25398-32-7	<184(total)[a]	
			<61 (total)[a]	
			171	
			<61 (total)[a]	
Epichlorohydrine (ECH)	Crosslinking agent	106-89-8	2.3	
2,3-Dichloro-1-propanol (2,3-DCP)	Byproduct of ECH	616-23-9		
1,3-Dichloro-1-propanol (1,3-DCP)	Byproduct of ECH	96-23-1	58	
3-Chloro-1,2-propanediol (3-CPD)[b]	Byproduct of ECH	96-24-2		
Triethyleneteramine (TETA)	Starting material	112-24-3		
			57	

[a] K&H notes that these impurities consist of a range of congeners with C_8 being the most abundant, constituting one-half or more of the various congeners. Therefore, if the C_8 is not detected, the other congeners will not be detected. Rather than using one-half of the detection limit of the C_8 congener to represent the residual level of each congener in the 100% migration calculations, the notifier suggests using the detection limit of the C_8 congener to represent all of the congeners(see FCN 314 update dated February 20, 2003). We do not agree with this approach. Instead, we will use the appropriate LODs to represent each set of congeners present in the FCS.

[b] Hydrolysis product of 1,3-DCP.

Use, Use Level, and Intended Technical effect

The intended use and technical effect of the FCS is discussed in FDA Form 3480, Part II, Section D, Parts 1-3 of FCN 487 and Attachment 6 of FCN 314.[3] The notifier intends to use the FCS as an oil/grease resistant sizing agent employed at the size press. The maximum use level of the FCS is 0.5% by weight of the dry paper and paperboard. The FCS is intended for use in contact with all food types (I-IX) under conditions of use B-H, as described in Tables 1 and 2 of 21 CFR 176.170(c), respectively. Data supporting the technical effect of the FCS were previously reviewed and found to be adequate.[3]

Migration Tests

1,3-Dichloropropanol and 3-Chloro-1,2-propanediol

The notifier performed migration testing on samples of paper (basis weight of 53 mg/in^2) coated with the FCS (coating rate was equivalent to 0.6% by weight of the dry paper). Control samples treated with water were also prepared and subjected to migration testing. Nineteen 2.5 by 2.5 inch squares, having a total surface are of 119 in^2 (single sided), were separated by metal screens and submerged in 240 mL of either 10% ethanol or corn oil. The samples were subjected to migration testing conditions that support conditions of use B-H (2 hours at 100 °C followed by 238 hours at 40°C). The volume to surface area ratio was 2 mL/in^2. Although the volume to surface area ratio is below our recommended 10 mL/in^2, the notifier states that there was no evidence of precipitation. The migration samples were analyzed after 2 hours, 24 hours, and 10 days for 1,3-DCP and 3-CPD using a gas chromatograph equipped with an electron capture detector. A detailed description of the analytical method and migration experiments are in Attachment 2 of the notification. The notifier did not analyze the migration solutions for any of the other impurities listed in Table 2.

The notifier analyzed seven standard solutions of 1,3-DCP and 3-CPD ranging in concentration from 0.00275 µg/mL to 0.005 µg/mL and plotted the response against concentration. Calibration solutions were prepared in diethyl ether and acetonitrile.[6] The correlation coefficients for the 1,3-DCP and 3-CDP calibration curves are greater than 0.9996 and 0.9986, respectively.

The sample extracts, after appropriate workup, were analyzed in triplicate for 1,3-DCP and 3-CPD. The 1,3-DCP and 3-CPD were not detected above the LOD of 0.001 µg/in^2 in the 10% ethanol migration solution. 1,3-DCP was not detected above the LOD of 0.001 µg/in^2 in the corn oil extracts. 3-CPD was detected at an average concentration of 0.020 µg/in^2 in the 2-hours corn oil migration solutions and 0.013 µg/in^2 in the 10-day corn oil migration solutions.

The migration experiments conducted with 10% ethanol were validated by spiking the migration solutions with 1,3-DCP and 3-CPD at the LOD (0.001 µg/in^2).[7] The analytes are clearly detectable at this level.

The corn oil experiments were validated by spiking the migration solutions with 1,3-DCP at the LOD (0.001 µg/in^2) and 0.01, 0.20, and 0.40 µg/in^2 of 3-CPD before work-up. The 1,3-DCP was detected in the samples. The average percent recoveries for 3-CPD for the 0.01, 0.20, and 0.40 µg/in^2 spikes are 81%, 103%, and 76%, respectively. The percent recoveries are acceptable.

The notifier relies on migration experiments submitted in FCN 314 to estimate exposure to

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6 During workup, the 10% ethanol food simulant is removed and replaced with diethyl ether. The corn oil food simulant is extracted with acetonitrile. The calibration curves were generated using either ether or acetonitrile solutions of the analytes.

7 Although not clearly stated in FCN 487, review of the validation data in FCN 487 and the analytical method in FCN 314 indicate the migration solutions were spiked before work-up.

The migration experiments were found adequate to support FCN 314.[3] As discussed above, the data provided in FCN 314 are suitable to support the residual levels provided in the current FCN. The analytical methods and data for these measurements were reviewed in detail during our review of FCN 314; we will not comment further on the analyses.[3] The migration levels for these impurities, as taken from the chemistry memorandum on FCN 314 are summarized in Table 2.[3]

Table 2. Migration values for TETA,

	10% ethanol <M> (µg/kg)	Corn oil <M> (µg/kg)
	<1	<1 (50% ethanol)
	<5	<5
	0.2	0.9

a. ½ the LOD was used in exposure calculations based on the non-detection of in FCN 314. This value was used in error. We will use the LOD for to estimate exposure.
b. The notifier provided migration results for in 10% ethanol. Data in corn oil was not provided due to difficulties in the analysis of in corn oil. The notifier claims that since the solubility of in 10% ethanol is significantly higher than that of corn oil, a worse-case migration in a fatty food simulant could be represented by the 10% ethanol solvent. We concur with the notifier's claim.

Impurity Analysis

Oligomers, Fluorinated Telomer Iodide, Epichlorohydrin, 2,3-Dichloro-1-propanol, and Perfluorooctanoic Acid

The FCS was analyzed for oligomers, fluorinated telomer iodide, epichlorohydrin, 2,3-dichloro-1-propanol, and perfluorooctanoic acid. The analytical methods and data for these measurements were reviewed in detail during our review of FCN 314; we will not comment further on the analyses.[3] As discussed above, we agree that the supporting data for the analysis of the impurities in the FCS provided in FCN 314 can be used to support the residual levels provided in FCN 487. The residual levels for these impurities are summarized in Table 1.8

was not identified as an impurity in FCN 314, but was identified as an impurity in this submission and in FCN 467. The notifier did not provide supporting data for the analysis of in this submission but responded to our request for data supporting the content of the FCS by incorporating by reference the analyses found in Attachment 1 of A review of this data revealed some minor deficiencies that the notifier corrected

8 Note, the residue levels reported on page 5 of the FCN for the fluorinated telomer iodide, are totals encompassing all congeners, C_8, C_{10}, and C_{12}.

in their 3/16/05 update to FCN 487.

A 1 g sample of freeze-dried FCS was extracted with methanol overnight, filtered and analyzed in duplicate for [redacted] using electrospray LC/MS/MS. The notifier prepared six standard solution of [redacted] ranging in concentration from 0.2 to10 ng/mL. The correlation coefficient for the [redacted] calibration curve is 0.9926.

Re-evaluation of the data provided in FCN 467 and the 3/16/05 update indicates that the residual [redacted] concentration in the FCS is typically 57 ppm (5733 ng/mL) in the finished FCS.

The analytical measurements were validated by spike and recovery experiments. A second batch of the FCS was analyzed for [redacted] (2385 ng/mL) and spiked with 5000 ng/mL [redacted] The amount of [redacted] detected in the spiked sample was 6060 ng/mL, or 73% recovery [(6060-2385)/5000*100]. Duplicate analyses were performed. The percent recovery is acceptable.

Exposure Assessment

1,3-DCP and 3-CPD

The exposures to 1,3-DCP and 3-CPD are based on the highest migration values obtained for each of the solvents used in the migration experiments or the appropriate LOD[9], the food-type distribution factors for paper and paperboard ($f_{aqueous + acidic} = 0.59$, $f_{alcoholic + fatty} = 0.41$), and the consumption factor (CF) for specialty paper of 0.05.[10] A sample calculation estimating the dietary concentration (DC) of 1,3-DCP is shown below.

$$DC = CF \times \langle M \rangle_{[(faqueous + acidic \times \langle M \rangle 10\% \text{ Ethanol}) + (falcohol + fatty \times \langle M \rangle \text{Corn oil})]} \quad \text{(Eq. 1)}$$

$$= 0.05\ [(0.59 \times 0.1 \text{ ppb}) + (0.41 \times 0.1 \text{ ppb})] = 0.005\ \mu g/kg \text{ or } 5 \text{ pptr}$$

The estimated daily intake (EDI) for 1,3-DCP is calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = 5 \text{ pptr} \times 3 \text{ kg food/p/d} = 15 \text{ ng 1,3-DCP/p/d} \quad \text{(Eq. 2)}$$

The DC and EDI of 3-CPD are calculated in a similar fashion.

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9 The concentration of 1,3-DCP and 3-CPD in $\mu g/in^2$ is converted to concentration in food by multiplying by our standard assumption that 10 g of food contacts 1 square inch of food packaging. For example, 0.02 $\mu g/in^2$ x 1 in^2/10 g food x 1000g/kg gives a concentration of 3-CPD in food of 2 ppb.

10 A CF of 0.05 is representative of specialty paper. See the chemistry memorandum for FCN 255 dated September 4, 2002 (effective September 5, 2002; A. Bailey to H. Macon) and the chemistry memorandum for FCN 59 dated August 1, 2000 (effective August 16, 2000; R. Costantino to E. Machuga).

[redacted] and TETA

The exposures to [redacted] and TETA are based on migration results provided in FCN 314. These migration experiments were reviewed in detail during our review of FCN 314[3] and are appropriate for use in estimating exposure in the current submission, see Table 2. The DCs for TETA and allyl alcohol are estimated by substituting their respective LODs from Table 2 into Equation 1. The [redacted] consists of a range of congeners with C_8 being the most abundant (constituting one half or more of the various congeners).[11] In order to estimate exposure to all [redacted] in the FCS, we multiplied <M> by a factor of two and substituting these numbers into Eq. 1.

Oligomers, Fluorinated Telomer Iodide, [redacted] Epichlorohydrin, 2,3-Dicloro-1-propanol, and Perfluorooctanoic Acid

The exposure estimates to the oligomers, fluorinated telomer iodide, [redacted] epichlorohydrin, 2,3-dichloro-1-propanol, and [redacted] are based on the assumption of 100% migration of their residual levels to food and the following: their respective residual levels from Table 1, our standard assumption for the average basis weight of food-contact paper and paperboard (50 mg/in^2), the maximum use level of the FCS (0.5%, or 0.005 mg FCS/mg paper), our standard assumption that 10 grams of food contacts 1 in^2 of food packaging, and the consumption factor for specialty paper and paperboard (0.05). An example of the calculation using epichlorohydrin (ECH, residue level 2.3 ppm) is shown below.

$$DC = 0.05 \times \left(\frac{2.3\,mg\,ECH}{1000\,g\,FCS}\right)\left(\frac{1\,g\,FCS}{1000\,mg\,FCS}\right)\left(\frac{0.005\,mg\,FCS}{1\,mg\,paper}\right)\left(\frac{50\,mg\,paper}{1\,in^2}\right)\left(\frac{1\,in^2\,paper}{10\,g\,food}\right)\left(\frac{1000\,g\,food}{1\,kg\,food}\right)\left(\frac{1000\,ug}{1\,mg}\right) = 0.003\,ppb \qquad (Eq.3)$$

The EDIs for these impurities are estimated by substituting their respective DCs into Equation 2. The exposure estimates to the oligomers, fluorinated telomer iodide, [redacted] epichlorohydrin, and 2,3-dicloro-1-propanol, perfluorooctanoic acid are summarized in Table 3.

[redacted]

As described above and in the notification, the fluorinated impurities consist of a number of congeners, C_8, C_{10}, C_{12}, with the C_8 isomers representing more than 50% of these congeners. In order to estimate exposure to the total [redacted] we have we multiplied the residual level of 57 ppm by two, giving 114 ppm. Substituting 114 ppm into Equation 3 provides the DC of the [redacted] 0.14 ppb.

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11 K&H notes that [redacted] consists of a range of congeners with C_8 being the most abundant (constituting one half or more of the various congeners). K&H supports the nature of these impurities in the February 20, 2003 submission to FCN 314.

Table 3: Exposure Estimates for Impurities in the FCS

Impurity	DC (ppb)	EDI (µg/p/d)	EDIs from FCN 314 (µg/p/d)
FCS oligomers	0.5	1.5	
C_6-C_{18} Fluorinated telomer iodides (FTI)	0.23	0.69	
	0.27	0.81	
	0.076	0.23	
	AIBN Regulated in	§ 176.170	
	0.076	0.23	
	0.056	0.17	
Epichlorohydrine (ECH)	0.003	0.009	
2,3-Dichloro-1-propanol (2,3-DCP)	0.01	0.03	
1,3-Dichloro-1-propanol (1,3-DCP)	0.005	0.015	
3-Chloro-1,2-propanediol (3-CPD)	0.044	0.13	
Tetraethylene tetraamine (TETA)	0.05	0.15	
	0.071	0.21	
	0.14	0.43	
	Essentially zero		
	Essentially zero		
	Essentially zero		

Cumulative EDIs

Oligomers

As stated above, the exposure to the oligomers is expected to be no greater than that calculated in FCN 314. Since the use of the FCS as described in this notification is substitutional for the use described in FCN 314, the CEDI for the oligomers of the FCS will remain at 1.5 µg/p/d.

Impurities

In FCN 314, exposures to the fluorotelomer iodides, fluorinated iodides, epichlorohydrine, and 2,3-DCP were estimated using our wet-end paper model, which provided very small exposures to these compounds. As described in FCN 487, the FCS is applied to paper as a coating at the size press, which results in higher exposures to these impurities. Although the use of the FCS described in FCN 487 is substitutional, exposures to these impurities, as calculated above, are worst-case estimates and would subsume those provided in FCN 314. Exposures to the 1,3-DPC, 3-CPD, and TETA, as calculated above, should also be considered worst-case estimates for the use of the FCS as a paper additive.

At this time, we do not have a CEDI for The working group should take into account the EDI of 0.21 µg/p/d when preparing their CEDI.

Conclusion

The chemistry and exposure data submitted in support of this FCN were evaluated and found to be adequate to support a safety decision.

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Kirk Arvidson, Ph.D.

AD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: June 10, 2005

From. Division of Food Contact Notifications
Chemistry Review Group II

Subject: FCN 487: Request for evaluation of regulated and authorized perfluoro materials for the presence of fluorinated iodohydrins, fluorinated epoxides, and the fluorinated alcohol by-products.

To: Division of Food Contact Notifications
Regulatory Group II
Attn: P. Honigfort, Ph.D

Toxicology verbally requested that Chemistry determine if the [redacted] identified as impurities in FCN 487 are present in any of the currently authorized or regulated perfluorocarbon materials.

[redacted]

Background

[redacted]

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Formation of Compounds **1-3**

[redacted]

Conclusion

produce a grease-proofing agent. Therefore, compounds **1-3** are unique to the FCS described in FCN 487 and are not expected to be present in other grease-proofing agents.

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Kirk Arvidson, Ph.D.

AD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: July 6, 2005

From. Division of Food Contact Notifications
Chemistry Review Group II

Subject. FCN 487: Additional information supporting the large increase in number-average molecular weight of the FCS described in FCN 487 and FCN 314

To. The record, FCN 487

During our preliminary review of Food Contact Notification (FCN) 487, we noted a significant change in the manufacturing process from that described in FCN 314. Because of the change in the manufacturing process, we requested the notifier provide new molecular weight data on the FCS. The notifier provided the requested data in the 2/14/05 update. Although the notifier indicates that there are no significant changes to the low molecular weight fraction of the current FCS when compared to that reported in FCN 314, we noted that the number-average molecular weight of the FCS manufactured by the method described in FCN 487 increased substantially from 24,368 Daltons to 188,359 Daltons. In our original memorandum on FCN 487 dated 4/26/2005, we proposed that the significant increase in the number-average molecular weight was due to a modification to the way the

Information provided in the 6/25/2005 update to FCN 518 (Use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine perfluorinated as a oil/grease-resistant sizing agent for food contact paper and paperboard in microwave applications) indicates that the modification to the method used to add the may not be the only reason for the increase in the number-average molecular weight. The notifier notes in the 6/25/2005 update to FCN 518 that may also affect the number-average molecular weight. Since the number-average molecular weight emphasizes lower molecular weight species more than the weight-average molecular weight, removal of these low molecular weight species would serve to increase the number-average molecular weight of the FCS identified in FCN 487. Review of the molecular weight data provided in FCN 487 and in the 6/25/2005 update to FCN 518, shows the absence of peaks due to the removal of low molecular weight materials from the FCS. Therefore, the also serves to

increase the number-average molecular weight of the FCS.

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Kirk Arvidson, Ph.D.

SOLENIS FCN 518

Part II — CHEMISTRY INFORMATION

Section **A - IDENTIFICATION OF THE FOOD CONTACT** SUBSTANCE

Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propen-1-01, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2. CAS Registry Number

464178-90-3

3. Trade or Common Name

PPD D-1085; Impress™FP100

4. Other Chemical Names (IUPAC, etc.)

n/a

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

See Attachment **1** to FCN **314** for chemical structure. The chemical formula is:

$H\text{-}(C_2H_5N)_{x1}\text{-}(C_5H_{11}NO_2)_{x2}\text{-}(C_5H_{10}NOCl)_{x3}\text{-}(C_5H_9NOCl)_{x4}\text{-}(C_5H_{10}NON\text{-}x\ link)_{x5}\text{-}(C_{11\text{-}23}H_{10}NOF_{13\text{-}37})_{x6}\text{-}(C_8H_{17}NO_3Cl)_{x7}\text{-}C_{12\text{-}24}H_{12}N\text{-}x\ linkF_{13\text{-}37}$

Mw = **3,067,499** Daltons
Mn = **24.368** Daltons

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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

^{13}C NMR and ^{1}H NMR spectra are included in Attachment **2** to FCN **314.**

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Section B - MANUFACTURE

Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

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Section B - MANUFACTURE - Continued

. **List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.**

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
Epichlorohydrin	106-89-8		
,3-Dichloro-1-propanol	616-23-9		
1,3-Dichloro-2-propanol	96-23-1		
3-Chloro-1,2-propanediol	96-24-2		
Triethylenetetramine	112-24-3		
Allyl alcohol	107-18-6		

Section C - PHYSICALICHEMICAL SPECIFICATIONS
Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Weight percent polymer below 1000 Daltons = 3%
Weight percent polymer below 500 Daltons is not available

(See Attachment 7 to FCN 314, pp. 9, 128-140.)

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil/grease resistant sizing agent at levels up to 0.5% employed either prior to the sheet forming operation or at the size press for paper and paperboard intended for use in microwave heat-susceptor packaging.

2. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
The FCS is intended for use as an oil/grease resistant sizing agent at levels up to 0.5% employed either prior to the sheet forming operation or at the size press for paper and paperboard intended for use in microwave heat-susceptor packaging.	All food types (Types I – IX)	Susceptor microwave packaging.

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil/grease/fat and water stains can weaken paper, making it susceptible to punctures and tears. In addition, the stains hurt the print quality of the paper and can make the bag appearance undesirable to the consumer. When the oil/grease/fat or water contained in the paper baglcontainer wets the outer surface of the bag/container, the surfaces the paper comes in contact with can become slippery, creating a safety hazard. Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water.

Data demonstrating the technical effect of the FCS are provided in Attachment 6 to FCN 314. Three different types of tests were conducted (Kit number, Pet Food Test, and HST), comparing the FCS to four of the leading commercial products in the market. Three batches of the FCS, as well as an untreated paper control, were compared to these commercial products.

The minimum amount needed to achieve the intended technical effect in microwave susceptor applications is 0.1% - 0.5%.

Section E - *STABILITY DATA*
See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

See Attachment 2 for a report entitled 'Characterization and Migration of Potential Thermal Degradation Products under Microwave Susceptor Heating of Impress™ FP-100 Treated Paper Sheets." As shown therein. Impress™ FP-100 was washed with water/Freon to move non-polymer components and dried. Thermal gravimetric analysis (TGA) was carried out in a flow through furnace tube at temperatures up to 200°C, 225°C, and 240°C while approximately 100 ml/minute of air was passed through the tube into a nitrogen cooled collection trap. Weight loss was measured after each of these temperatures were attained. At 220°C, the temperature more associated with microwave popcorn cooking on a susceptor, approximately 8.8% of the polymer was lost. The material collected in the cooled trap was analyzed by gas chromatography/mass spectrometry (GCIMS), and by nuclear magnetic resonance (NMR).

The compounds identified by GC/MS were of the type $H(CF_2)_nCF_3$ where n=7-11, and perfluoroalcohols, as set forth in the following table. IMR identified the potential oligomeric content in the trapped material.

2 List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable.
ess the amount of any breakdown products that migrate to food and ensure that exposures to these substances are
.ıressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure
1H-perfluorooctane (considered a surrogate for all $H(CF_2)_nCF_3$ compounds where n=7-11)	**335-65-9**	$H(CF_2)_{7-11}CF_3$
3-(perfluorooctyl)prop-2-enol	**2340-84-3**	$F(CF_2)_8CH{=}CHCH_2OH$
1H, 1H, 2H, 2H-heptadecafluoro-n-decanol	**678-39-7**	$F(CF_2)_8CH_2CH_2OH$
Oligomers	**N/A**	

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods ***(see Chemistry Recommendations II.D.5),*** skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime ***(see Chemistry Recommendations, Appendix II, Part 4).***

1. Migration Testing Option

See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

25 lbs/3000 ft^2 (26 mg/in^2) basis weight paper was used in the migration study. Untreated paper was used as a control and, although the FCS is requested for use at 0.5%, the samples consisted of the paper treated with 0.65% D-1085 on a dry weight basis. The extracts were analyzed for 1.3-DCP and 3-CPD. The control and sample sheets were folded up at the edges to form a "tray" to contain the food simulant. Heat susceptors were then glued to the bottoms of the "trays" so that the controls and treated paper were between the heat susceptor and the food simulant. The results were not factored down to account for the requested 0.5% use level. (See Attachment 3 or migration data.)

A second migration study was conducted on paper treated with 0.65% FCS. The test was carried out as described above and the extracts were examined for the migration of the decomposition products listed in Part II, E.2.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mY in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Corn oil was added to the "trays" and the filled trays containing –5 g oil/in^2 were placed in a 700 watt microwave oven and heated on "high" or 5 minutes.

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate) ($\mu g/in^2$)	Average Migration (average of replicates)
25 lb/3000 ft^2 uncoated paper sheets treated at 0.65% dry weight FCS	1,3-DCP	Corn oil	5 minutes at 700 watts	0.013 $\mu g/in^2$ 0.024 $\mu g/in^2$ 0.028 $\mu g/in^2$	0.022 $\mu g/in^2$
	3-CPD	Corn oil	5 minutes at 700 watts	0.051 $\mu g/in^2$ 0.072 $\mu g/in^2$ 0.088 $\mu g/in^2$	0.070 $\mu g/in^2$
25 lb/3000 ft^2 uncoated paper sheets treated at 0.65% dry weight FCS	1-H-Perfluorooctane	Corn oil	5 minutes at 700 watts	<0.50 $\mu g/in^2$	<0.50 $\mu g/in^2$
	1H, 1H, 2H, 2H-Heptadecafluoro-n-decanol	Corn oil	5 minutes at 700 watts	<0.50 $\mu g/in^2$	<0.50 $\mu g/in^2$
	3-(Perfluorooctyl) prop-2-enol	Corn oil	5 minutes at 700 watts	<0.50 $\mu g/in^2$	<0.50 $\mu g/in^2$

Section F - MIGRATION LEVELS IN FOOD - Continued

Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Analyte	Corn oil	
	Amount added	% Recovery
1,3-DCP	0.005 µg/ml	55
	0.01 µg/ml	54
	0.02 µg/ml	59
3-CPD	0.015 µg/ml	78
	0.030 µg/ml	77
	0.060 µg/ml	77
1-H-Perfluorooctane	0.52 µg/in^2	detected
1H, 1H, 2H, 2H-Heptadecafluoro-n-decanol	0.49 µg/in^2	76
3-(Perfluorooctyl)prop-2-enol	0.48 µg/in^2	117

'Migration Calculation Option

Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on PDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

The following calculations assume (1) 26 mg paper/in^2 treated with 0.5% FCS, and (2) 100% migration to 5 g food/in^2.

FCS

As explained in FCN No. 314, Attachment 7, p. 9, the maximum level of low-molecular weight (<1000 Daltons) oligomers of the FCS is 410 ppm. However, based on the thermal degradation data presented in Attachment 2, additional low-molecular weight oligomers appear to be generated during the intended use of the FCS. More specifically, Hercules performed a thermal gravimetric analysis (TGA) of the FCS and then analyzed the volatile material collected in the cold trap by NMR. The NMR analysis shows approximately 0.8% of perfluoro-containing oligomers in the TGA tube. We note, however, that this value represents a worst-case, as the NMR integral used to determine this value would include non-oligomeric components. Nonetheless, assuming as a worst-case that the FCS contains 0.8% low-molecular weight oligomers under the intended temperatures of use, the maximum migration of these oligomers is calculated as follows:

26 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.008 mg oligomers/mg FCS ÷ 5,000 mg food/in^2 = 2 x 10^{-7} mg oligomers/mg food = 200 ppb

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See Attachment 4 to this FCN.

Section G- ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations Sections II.E and Appendix IV

EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

$$\begin{aligned} EDI &= DC \times 3 \text{ kg food/p/d} \\ &= CF \times \langle M \rangle \times 3 \text{ kg food/p/d} \\ &= CF \times [(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})] \times 3 \text{ kg/p/d} \end{aligned}$$

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See Attachment 5.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: September 23, 2005

From: Division of Food Contact Notifications
Chemistry Review Group II

Subject: FCN 518: Hercules Inc., through Keller and Heckman, L.L.P., submissions dated 4/25/2005 and 6/22/05 for the use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine as an oil/grease-resistant sizing agent in paper and paperboard intended for use in microwave heat-susceptor packaging.

To: Division of Food Contact Notifications
Regulatory Group II
Attn: V. Gilliam, Ph.D.

Hercules Inc., through Keller and Heckman, L.L.P., submitted this food contact notification (FCN) for the use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine as an oil/grease-resistant sizing agent in paper and paperboard intended for use in microwave heat-susceptor packaging. The food contact substance (FCS) is intended to be added to the paper prior to the sheet forming operation or at the size press.

Regulatory Status

The FCS is not currently regulated in 21 CFR 170-199 but it is the subject of two effective FCNs (FCN 314 and 487). The FCS is similar to the FCSs described in FCN 59[1] (effective 8/16/00) and FCN 255[2] (effective 9/5/02), submitted by Ciba Specialty Chemicals Corporation. The notifier also submitted FCN 467 for the use of the FCS as a grease-proofing agent in microwave susceptor packaging. FCN 467 was withdrawn due to chemistry deficiencies. The notifier has incorporated by reference portions of FCN 314, FCN 467, and FCN 487.

Identity and Manufacture

Information on the identity of the FCS is contained in FDA Form 3480, Part II Section A, and Attachments 1 and 2 of FCN 314.[3]

[1] Chemistry memoranda for FCN 59 dated August 1, 2000 and August 10, 2000; R. Costantino to E. Machuga.
[2] Chemistry memorandum for FCN 255 dated September 4, 2002; A. Bailey to H. Macon.
[3] This information was reviewed in the chemistry memorandum dated 3/17/03 from S. Elyashiv-Barad to V. Gilliam on FCN 314.

CAS name: 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

CAS Reg. No.: 464178-90-3

Other name:

Chemical Structure[4]:

The notifier provided supporting data for the molecular weight data and revised molecular weights for the FCS in Attachment 1 of the 6/22/05 update to the notification. The revised numbers are shown above.

Characterization

The notifier incorporated by reference the carbon-13 and proton NMR spectra for the FCS from Attachment 2 of FCN 314.[3] The data provided in FCN 314 are applicable to the material identified in this notification. The spectra are consistent with the proposed structure of the FCS.

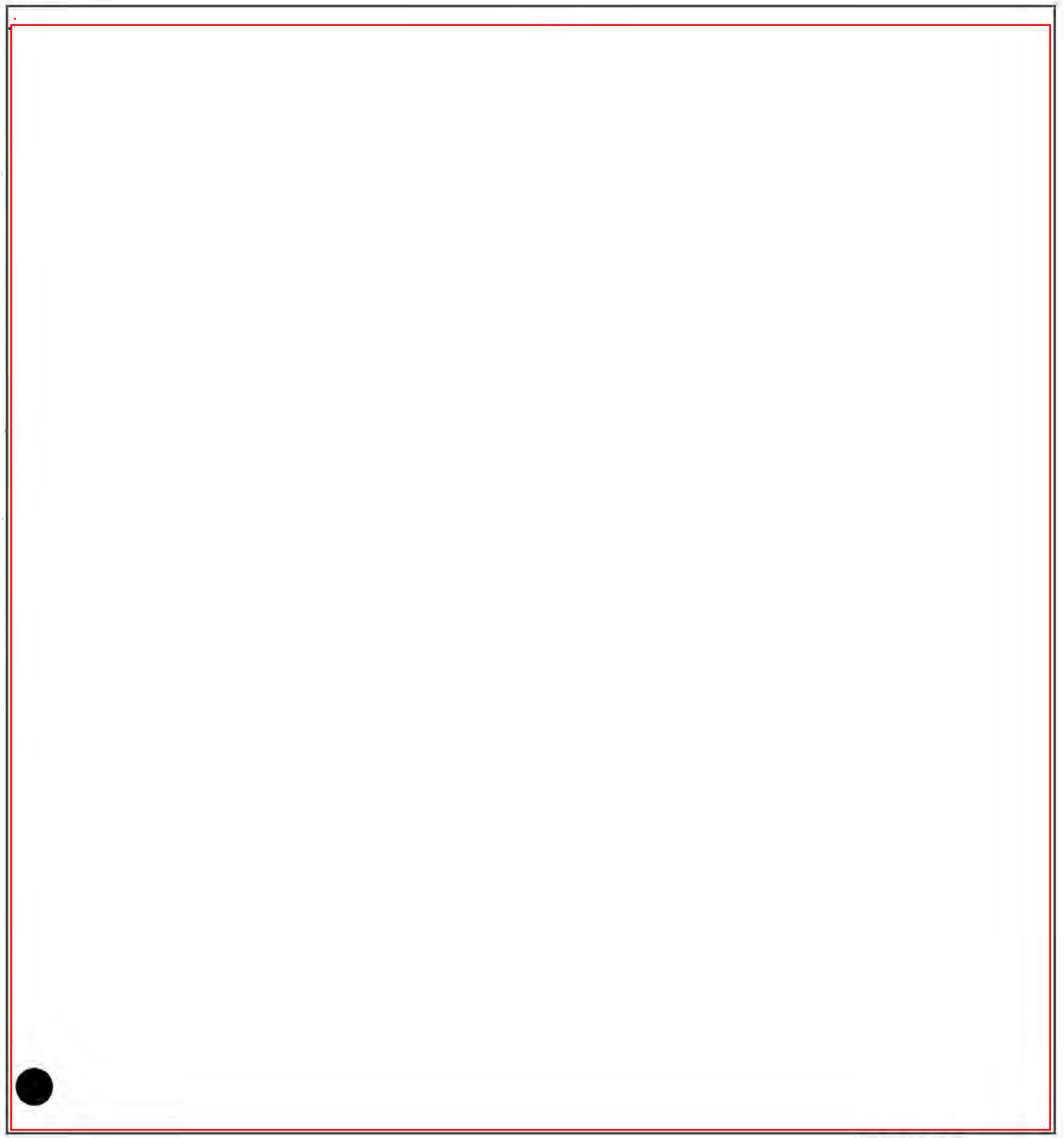
[4] We note that the molecular formula listed on page 3 of the FCN contains an error. We have reviewed the molecular structure for the FCS provided in Attachment 1of FCN 487 and the manufacturing scheme and believe that

Manufacture

Impurities

Information on impurities in the FCS is contained in FDA Form 3480, Part II Section B.3, of this submission. Typical residual levels of each impurity as cited in FCNs 518, 487, and 314 are provided in Table 1.

[5] Chemistry memorandum for FCN 487 dated April 26, 2005; K. Arvidson to P. Honigfort.



provided on page 5 of the FCN. The notifier was asked to verify the residual level of AA and provide appropriate updates, including new batch analyses supporting the correct residual level of AA. The notifier responded in the 6/22/05 update that the 316-ppm AA level was determined in a sample having a solids content of 20% (Attachment 3, page 44). The validation experiments were conducted on a sample having a solids content of 15% and an AA level of 1853 ppm (Attachment 3, page 47). Because the 316-ppm level of AA was not validated, and that the notifier found varying levels of AA in different samples, the notifier revised the FCN to reflect a residual level of 1853 ppm AA.

Intended Technical Effect/Use/Use Level

The FCS is intended for use as an oil/grease-resistant sizing agent at levels up to 0.5% in paper and paperboard intended for use in microwave heat-susceptor packaging. The FCS is intended to be added to the paper prior to the sheet-forming operation or at the size press. The notifier provided data in Attachment 6 of FCN 314 supporting the grease-resistant properties of the FCS.[3]

Stability

The notifier indicates that the FCS is thermally unstable under the intended conditions of use. The notifier provided a study on the characterization and migration of thermal degradation products in Attachment 2 of the notification.

Thermogravimetric analyses of the FCS in air were conducted. Samples of the FCS were washed with a water/Freon mixture to remove non-polymeric materials and the samples were allowed to dry in air. Approximately 2 mg of the dried FCS was used for each analysis. The sample was heated from 22 °C to 360 °C at 82.9 °C/min. The samples reached 240 °C in approximately 3 minutes. Percent weight loss from the samples is reported as 8.8, 10.3, and 19.8 at 220, 225, and 240 °C, respectively.

During the preliminary review of this FCN, our environmental scientist questioned whether the 9% breakdown of the polymer would be expected under a real use scenario. Given that these experiments were performed on neat samples of the FCS, the TGA results would represent a worst-case scenario for the decomposition of the FCS under microwave heating. Under actual use conditions, a majority of the FCS applied to the popcorn bag would not be in contact with the susceptor-heated oil. Rather, it would be exposed to large volumes of steam (100 °C). Examination of the TGA curve shows less than 5% weight loss of the polymer at 100 °C. Therefore, we would expect 5% or less of the FCS applied to a popcorn bag to breakdown during use.

Migration Tests and Impurity Analyses

Oligomers in the FCS

The FCS was previously analyzed for oligomers. The analytical methods and data for these measurements were reviewed in detail during our review of FCN 314; we will not comment further on these analyses.[3] Since the method of manufacture has not changed substantially from

that reported in FCNs 314 and 487, we believe that the supporting data for the analysis of the FCS for oligomers provided in FCN 314 and 487 can be used to support the residual levels cited in this FCN. The concentration of the oligomers was determined to be approximately 1.4% in these earlier studies. The notifier refers to these FCS-derived oligomers as TETA-oligomers (TETA-oligomers does not include fluorinated oligomers. As stated in FCN 314, we believe exposure to the fluorinated oligomers would be accounted for in the exposure estimates to the [redacted], discussed below.)

In order to determine the concentration of additional TETA-oligomers formed during microwave-heating, the notifier heated a 1-3 g sample of the dry FCS in air using a TGA equipped with a quartz U-tube.6 The U-tube was immersed in liquid nitrogen to trap the volatile gasses as they were swept out of the TGA oven. The condensate in the U-tube was solublized in deuterated hexafluoroisopropanol and quantified by NMR spectroscopy against the internal standard hexamethyldisiloxane. Analysis of the spectra showed signals associated with TETA at 3.0-4.0 ppm.

The notifier quantified the TETA-oligomers using the proton NMR integrals from the standard (hexamethyldisiloxane) and the TETA-oligomers, the respective formula weights of the standard and TETA-oligomers,[7] the amount of sample used and the amount of standard added to the sample, and the weight-percent of TETA containing materials in the FCS. A description of the validated procedure for this type of analysis is on page 18 of Attachment 3. From the integrals of the TETA peaks and the internal standard, it was determined that there is approximately 0.8 g of new TETA-oligomers per 100 g of FCS (8000 ppm) produced during heating of the FCS under conditions simulating microwave oven conditions. A detailed calculation is provided on page 13 of Attachment 2 of the notification.

Allyl Alcohol

The concentration of allyl alcohol in the finished FCS was determined by passing a sample of the FCS, as an aqueous dispersion, through an Extrelut QE SPE column. The polymeric materials were adsorbed to the column packing and the remaining compounds were eluted from the column with ethyl acetate. The ethyl acetate solution was analyzed using a GC equipped with a flame ionization detector (FID). The notifier prepared five allyl alcohol standards ranging in concentration from 1.254 to 156.8 µg/mL wet FCS and analyzed them by GC/FID. The correlation coefficient for the resulting calibration curve was 0.9999.

The notifier did not follow standard FDA recommendations for the validation of their analytical method (*i.e.,* spiking at 0.5, 1 and 2 times the detected level of the analyte). The notifier spiked a sample of the FCS that was previously determined to contain 1853 ppm allyl alcohol with an additional 940 ppm allyl alcohol, on a dry weight basis. The percent recovery for this experiment was 84%.

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6 Although the notifier speaks of a single sample, the wording of the FCN suggests they have analyzed multiple samples

7 The notifier used 1000 Daltons as an estimate for the molecular weight of the oligomers of concern, we agree with this assumption

The notifier analyzed two samples of the FCS for residual allyl alcohol and determined the concentration of allyl alcohol to be 316 μg/g (ppm) and 1853 ppm in each of the samples of the FCS, on a dry weight basis. Given the limited number of analyses and that the validation of the method was conducted at 940 ppm, as discussed by the notifier's 6/22/05 update, we cannot rely upon the average concentration of allyl alcohol in the FCS. Rather, we will use the 1853 ppm residual level as a worst-case concentration for allyl alcohol in the finished FCS.[8]

Fluorinated Telomer Iodide, Fluorinated Iodohydrin Intermediate, Fluorinated Epoxide Intermediate, Fluorinated Alcohols, Epichlorohydrin, and 2,3-Dichloro-1-propanol

The notifier used the residual levels of C_6-C_{18} fluorinated telomer iodides (FTI), C_6-C_{18} fluorinated iodohydrins (FI), C_6-C_{18} fluorinated epoxides (FE), C_6-C_{18} fluorinated alcohols (FA), ECH, and 2,3-Dichloro-1-propanol (2,3-DCP) to estimate exposures to these compounds. The residue levels are reported on page 5 of the FCN and are summarized in Table 1.[9] The analytical methods and data for these measurements were reviewed in detail during our review of FCN 314; we will not comment further on these analyses.[3] As was discussed in the chemistry memorandum on FCN 487[5], we do not believe that the current manufacturing process, differing slightly from that reported in FCN 314 and 487, will significantly alter the residual levels of these impurities. Therefore, supporting data for the analysis of the impurities provided in FCN 314 will be used to support the residual levels provided in FCN 518.

Migration of 1,3-Dichloropropanol and 3-Chloro-1,2-propanediol

Migration data for 1,3-dichloropropanol and 3-chloro-1,2-propanediol are provided in Attachment 3 of the notification and in Attachment 2 of the 6/22/05 update to the notification. The notifier performed migration testing on samples of paper (26 mg/in^2) coated with the FCS (0.65%, 13 lbs/ton) in accordance with our recommendations for microwave susceptors. Paper samples were folded to produce a 2.5 by 2.5 inch tray, total area 6.25 in^2. A microwave susceptor was glued to the bottom of the tray and the tray filled with 31 mL of corn oil (5 ml/in^2). The test cell and oil were heated in a 700 watt microwave on high for 5 minutes. Experiments on samples that had not been treated with the FCS were also performed. All analyses were performed in triplicate.

A 20 mL sample of oil from the test cell was extracted with two 5-mL volumes of acetonitrile. The acetonitrile extracts were combined, washed with hexanes to remove any residual oil, diluted to 10 mL in a volumetric flask, and analyzed for 1,3-DCP and 3-CDP using a gas chromatograph equipped with a halogen-specific detector. Calibration curves for 1,3-DCP and 3-CDP were generated using a series of standards ranging in concentration from 0.0022-0.02 μg 1,3-DCP/mL and 0.0023-0.057 μg 3-CPD /mL. The correlation coefficients for 1,3-DCP and 3-CDP are 0.9993 and 0.9989, respectively.

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8 (150 ug AA/1.0621 g sample)(100 g FCS/15 g solids)=940 ug AA/g dry FCS.

9 Note that the residue levels reported on page 5 of the FCN for the fluorinated telomer iodide, fluorinated iodohydrin intermediate, fluorinated epoxide intermediate are totals encompassing all congeners, C_8, C_{10}, and C_{12}. The congener mixture is reported as consisting of 50% or more of the C_8 congener.

The method was validated by spiking corn oil samples from the control samples with a known amount of each analyte at 0.5, 1 and 2 times the detected amount of the analyte. Verification of the results show that the percent recoveries ranged from 52-57% for 1,3-DCP and are approximately 74% for all 3-CDP spiking experiments. The percent recoveries cited for 1,3-DCP are low and to compensate, a correction factor of two will be applied to the migration values. The percent recoveries cited for 3-CPD are acceptable. See Attachment 2 of the 6/22/05 update for a full explanation of the spiking experiments and sample calculations.

Both 1,3-DCP and 3-CDP were detected in the migration solutions. 1,3-DCP showed an average migration of 4.4 μg/kg of food and 3-CDP had an average migration value of 14 μg/kg of food. To adjust for poor recovery of 1,3-DCP, we will double the concentration in food from 4.4 μg/kg to 8.8 μg/kg.

TETA

The notifier performed size exclusion chromatography (SEC) on samples of the FCS and collected the fraction that contained compounds with molecular weights below 1000 Daltons. This fraction as further analyzed by 1D and 2D NMR experiments, such as COSY (correlated spectroscopy), HMQC (heteronuclear multiple quantum coherence) and HMBC (heteronuclear multiple bond coherence), to determine the proton-NMR signal unique to TETA and TETA-containing materials.[3]

An SEC fraction containing materials with molecular weights of 1000 Daltons or less was concentrated and dissolved in hexafluoroisopropanol and a known quantity of the internal standard 1,4-dichlorobenzene was added to the sample. Using the proton NMR integrals from the standard and TETA, the respective formula weights of the standard and TETA, the amount of sample used and the amount of standard added to the sample, the weight-percent of TETA was determined in the FCS. Detailed sample calculations are provided on page 19 of Attachment 3 of the notification.

The method was validated by preparing a sample with a known quantity of TETA and the internal standard. Approximately 3 g of deuterated hexafluoropropanol was spiked with 36.4 mg of 1,4-dichlorobenzene and 12.1 mg of TETA and the proton NMR spectrum obtained. The NMR signals exclusive to TETA and the standard were integrated and the concentration of TETA determined. The recovery of TETA was estimated at 94%.

The concentration of TETA in the 1000 Dalton fraction was determined to be 0.28%. It was demonstrated in FCN 314 that approximately 3% of the FCS was low molecular weight oligomers. The concentration of TETA can be estimated by multiplying 3g oligomers/100 g FCS by 0.28 g TETA/100 g oligomers, giving 8.4×10^{-5} g TETA/g FCS. Since this number actually encompasses all materials below 1000 Daltons that contain the TETA moiety, it would represent a worst-case concentration of TETA in the finished FCS.

Non-TETA-Based Breakdown Products from Microwave Use

on page 13 of Attachment 2 of the notification.

In order to determine if hydrogen-terminated fluoroalkanes, fluoroalkanols and Rf-enol were migrating to food, the notifier performed a second migration experiment. The experiment was conducted as described in the entitled "Migration of 1,3-Dichloropropanol and 3-Chloro-1,2-propanediol," above. The notifer analyzed the migration solutions using solid phase microextraction (SPME) to selectively sample the headspace of the heated corn oil. The corn oil sample was placed in a headspace vial and the SPME fiber assembly placed into the headspace of the vial and the sample heated at 35°C for 15 minutes. The SPME fiber was injected into the inlet of a GC equipped with an electron capture detector (ECD) and the analytes thermally desorbed at 250° for 3 minutes. The notifier provided raw data and supporting chromatograms for each of these experiments in Attachment 2 of the FCN.

The notifier prepared and analyzed standard solutions of 1H-perfluorooctane (seven standards ranging in concentration from 0.061-1.3 µg/g, correlation coefficient of 0.9940), 1H, 1H, 2H, 2H-heptadecafluoro-n-decanol (seven standards ranging in concentration from 0.0903-0.2991 µg/g, correlation coefficient of 0.9988) and 3-(perfluorooctyl)prop-2-enol (seven standards ranging in concentration from 0.055-1.2 µg/g, correlation coefficient of 0.9821) as surrogates for the types of materials that are evolved during the microwave heating of the FCS.

The experiments were validated by spiking the corn oil migration solutions with each surrogate at a level equivalent to 100 µg/kg food and analyzing as described above. All spikes were detected. A recovery study was not conducted since the analytes were not detected in the migration solutions.

The notifier did not detect any hydrogen-terminated fluoroalkanes, fluoroalkanols and Rf-enol in the corn oil migration solutions.

Sodium Hypophosphate, Sodium Metabisulfate, and Sodium Sulfate
As stated in the manufacturing section, sodium hypophosphate, sodium metabisulfate, and sodium sulfate are water-soluble and would remain with the aqueous phase from reactor A. Therefore, the concentration of these materials in the finished FCS is estimated to be essentially zero.

Exposure Estimates

Oligomers
As noted above, the FCS is unstable and a small portion of the material breaks down to give additional TETA-oligomers. The NMR analysis of the TGA gasses demonstrated that approximately 8000 ppm of new TETA-oligomers are generated during simulated microwave heating. The exposure to these newly formed oligomers is estimated assuming 100% migration of the 8000 ppm TETA-oligomers to food and the following: a basis weight of 26 mg/in^2 for popcorn bags, the maximum use level of the FCS (0.5%, or 0.005 mg FCS/mg paper), our

standard assumption that 5 grams of food contacts 1 in^2 of microwave susceptor packaging,[11] and the consumption factor for microwave susceptor packaging (0.001). The equation used to estimate the DC of new TETA-oligomers and several other impurities is shown below (Eq. 1). Multiplying the DC by our standard assumption that a person consumes 3 kg of food per day gives an EDI of 0.6 μg new TETA oligomers/p/d.

$$DC = 0.001 \times \left(\frac{8000\text{mg TETA-oligomers}}{1000\text{g FCS}}\right)\left(\frac{1\text{g FCS}}{1000\text{mg FCS}}\right)\left(\frac{0.005\text{mg FCS}}{1\text{mg paper}}\right)\left(\frac{26\text{mg paper}}{1\text{in}^2}\right)\left(\frac{1\text{in}^2\text{ paper}}{5\text{g food}}\right)\left(\frac{1000\text{g food}}{1\text{kg food}}\right)\left(\frac{1000\text{ug}}{1\text{mg}}\right) = 0.2\text{ppb} \quad \text{(Eq.1)}$$

Exposure to oligomers from the use of the FCS in non-microwave susceptor paper and paperboard applications has been addressed in our chemistry memorandum on FCN 487.[5]

Allyl Alcohol, TETA, Fluorinated Telomer Iodide, Fluorinated Iodohydrin Intermediate, Fluorinated Epoxide Intermediate, Epichlorohydrin, 2,3-Dicloro-1-propanol, and Perfluorooctanoic Acid

The exposure estimates to allyl alcohol, TETA, fluorinated telomer iodide, fluorinated iodohydrin intermediate, fluorinated epoxide intermediate, epichlorohydrin, 2,3-dichloro-1-propanol, and perfluorooctanoic acid are based on the assumption of 100 % migration of their residual level to food. Substituting the appropriate residual levels from Table 1 for the 8000 mg of TETA-oligomers value in equation 1, provides their respective DCs. The DCs are summarized in Table 2, below.

The EDIs for these impurities are estimated by multiplying their respective DCs by our standard assumption that a person consumes 3 kg of food per day. The exposure estimates are summarized in Table 2.

1,3-DCP and 3-CPD

The exposures to 1,3-DCP and 3-CPD are calculated based on the average migration values obtained from the corn oil migration experiments provided in Attachment 3 of the notification and the consumption factor (CF) for microwave susceptor packaging, 0.001. A sample calculation estimating the dietary concentration (DC) of 1,3-DCP is shown below.

$$DC = CF \times \langle M \rangle_{\text{Corn oil}} \qquad \text{(Eq. 2)}$$

$$= 0.001 \times 8.8\ \mu g/kg\ \text{food} = 0.0088\ \mu g/kg \text{ or } 8.8\ \text{pptr}$$

The estimated daily intake (EDI) for 1,3-DCP is calculated by multiplying the DC by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = 8.8\ \text{pptr} \times 3\ \text{kg food/p/d} = 26\ \text{ng 1,3-DCP/p/d} \qquad \text{(Eq. 3)}$$

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11 FDA document *Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations,* April 2002.

Similarly, the DC and EDI of 3-CPD are estimated to be 0.014 ppb and 0.04 µg/p/d, respectively.

Cumulative EDIs

Oligomers

The current cumulative EDI of oligomers from previously authorized uses of this FCS is 1.5 µg/p/d. As stated above, this FCN represents a new use for the FCS and would increase the CEDI of the oligomers from 1.5 µg/p/d to 2.1 µg/p/d (1.5 µg/p/d + 0.6 µg/p/d).

Conclusion

The chemistry and exposure data submitted in support of this FCN were evaluated and found to be adequate to support a safety decision.

Kirk Arvidson, Ph.D.

Table 2: Exposure Estimates for Impurities in the FCS

Impurity	Typical residual (dry basis, mg/kg)	Basis of Exposure	DC (ppb) FCN 518	EDI (ug/p/d) FCN 518	EDI (µg/p/d) FCN 487	EDI (ug/p/d) FCN 314
FCS oligomers		From Microwave use	0.2	0.6	1.5	1.5
C_6-C_{18} Fluorinated telomer iodides (FTI)	<184(total)	100% of residual	0.0048	0.014	0.69	<0.008
Allyl alcohol	1853	LOD of method	0.05	0.15	0.81	0.021
C_6-C_{18} Fluorinated iodohydrins (FI)	<61 (total)	100% of residual	0.0016	0.005	0.23	<0.003
Tetramethyl succinonitrile (TMSN) Breakdown product from AIBN	171		-	AIBN Regulated in § 176.170		
C_6-C_{18} Fluorinated epoxides (FE)	<61 (total)	100% of residual	0.0016	0.005	0.23	<0.003
C_6-C_{18} Fluorinated alcohols (FA)	2989	Migration results FCN 518	0.1	0.3	0.17	0.12
ECH	2.3	100% of residual	0.00006	0.0002	0.009	0.0001
2,3-Dichloro-1-propanol (2,3-DCP)	8.2	100% of residual	0.00021	0.0006	0.03	0.0003
1,3-Dichloro-1-propanol (1,3-DCP)	9484	Migration results from FCN 518	0.0088	0.03	0.012	0.004
3-Chloro-1,2-propanediol (3-CPD)	3355	Migration results from FCN 518	0.014	0.04	0.13	0.03
TETA	<84	Residual level from 518	0.0022	0.007	0.15	0.08
Perfluorooctanoic acid (PFOA)	57	100% of residual	0.0015	0.005	0.2	Not determined
Perfluoroacid congeners	114	2 x PFOA residual level	0.003	0.009	0.4	Not determined
Perfluorinated alkanes		Migration Results FCN 518	0.1	0.3	-	-
Sodium hypophosphite monohydrate				Essentially zero	Essentially zero	Essentially zero
Sodium metabisulfite				Essentially zero	Essentially zero	Essentially zero
Sodium sulfate				Essentially zero	Essentially zero	Essentially zero

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Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

2-Propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2. CAS Registry Number

464178-94-7

3. Trade or Common Name

PPD D-1101

4. Other Chemical Names (IUPAC, etc.)

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

See Attachment 1 for chemical structure. The chemical formula is as follows:

(See Attachment 4, Appendix C for supporting molecular weight data)

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

NMR data are provided in Attachment 2.

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Section B - MANUFACTURE

Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

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Chemical Name	CAS Reg. No.	Function
Perfluorohexyl iodide	355-43-1	Starting material
Allyl alcohol	107-18-6	Starting material
Triethylenetetramine	112-24-3	Starting material
Epichlorohydrin	106-89-8	Starting material
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2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

The manufacturing process is included in Attachment 3.

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Section B - MANUFACTURE - Continued

5. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
Perfluorohexyl iodide	355-43-1		
Allyl alcohol	107-18-6		
Epichlorohydrin	106-89-8		
1,3-Dichloro-2-propanol (1,3-DCP)	96-23-1		
2,3-Dichloro-1-propanol (2,3-DCP)	616-23-9		
3-Chloro-1,2-propanediol (3-CPD)	96-24-2		
Triethylenetetramine (TETA)	112-24-3		

Ensure that exposures to these substances are addressed in Section II.G of this form.

00009

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

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Property	Max. Value	Min. Value	Individual Batch Values

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Weight percent polymer below 1000 Daltons = 2.543%
Weight percent polymer below 500 Daltons = 2.392%

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(See Attachment 4, Appendix C)

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil/grease resistant sizing agent in the manufacture of paper and paperboard at levels up to 0.5% by weight of the dry paper and paperboard intended for use in contact with food. Single use of the food-contact material is anticipated.

2a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
FCS in paper and paperboard up to 0.5% by weight of the dry paper and paperboard	All food types (Types I – IX)	B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

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Part II — CHEMISTRY INFORMATION - CONTINUED

State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil/grease/fat and water stains can weaken paper, making it susceptible to punctures and tears. In addition, the stains hurt the print quality of the paper and can make the bag appearance undesirable to the consumer. When the oil/grease/fat or water contained in the paper bag/container wets the outer surface of the bag/container, the surfaces the paper comes in contact with can become slippery, creating a safety hazard. Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water.

Data demonstrating the technical effect of a substance very similar to the FCS are provided in Attachment 6 to FCN No. 314. (The only difference between the FCS covered by FCN No. 314 and the present FCS is [redacted]); thus, the technical effect data are equally applicable to this FCS.)

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The minimum amount needed to achieve the intended technical effect is 0.05% - 0.5%.

Section E - STABILITY DATA

See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None.

Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

000014

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Approximately 50 mg/in^2 (50 lb/3000 ft^2) paper samples containing 0.5% FCS added at the wet end of the paper making process were used in the migration studies. Untreated paper prepared without the FCS was used as controls. The samples and controls were extracted by total immersion.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

The samples and controls were extracted with 10% ethanol-in-water to simulate contact with aqueous, acidic, and low alcohol (≤15% by volume alcohol) foods. To simulate contact with fatty foods, either corn oil or 50% ethanol-in-water was used. A 2 ml/in^2 simulant volume to surface area ratio, counting the area of one side of the samples, was used.

The samples and controls were exposed to the food simulants at Condition of Use B test conditions, *i.e.,* 100°C for 2 hours followed by 10 days at 40°C. No precipitation was noted in the resulting extracts under these conditions.

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Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued
Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
50 lb/3000 ft^2 uncoated paper sheets treated at 0.5% dry weight FCS	1,3-DCP	10% Ethanol	2 hours at 100°C	<1.3 ng/in^2 <1.3 ng/in^2 <1.3 ng/in^2	<1.3 ng/in^2
			2 hours at 100°C followed by 40°C for 238 hours	<1.3 ng/in^2 <1.3 ng/in^2 <1.3 ng/in^2	<1.3 ng/in^2
		Corn oil	2 hours at 100°C	<2.9 ng/in^2 <2.9 ng/in^2 <2.9 ng/in^2	<2.9 ng/in^2
			2 hours at 100°C followed by 40°C for 238 hours	<2.9 ng/in^2 <2.9 ng/in^2 <2.9 ng/in^2	<2.9 ng/in^2
	3-CPD	10% Ethanol	2 hours at 100°C	<3.6 ng/in^2 <3.6 ng/in^2 <3.6 ng/in^2	<3.6 ng/in^2
			2 hours at 100°C followed by 40°C for 238 hours	<3.6 ng/in^2 <3.6 ng/in^2 <3.6 ng/in^2	<3.6 ng/in^2
		Corn oil	2 hours at 100°C	<3.6 ng/in^2 <3.6 ng/in^2 <3.6 ng/in^2	<3.6 ng/in^2
			2 hours at 100°C followed by 40°C for 238 hours	<3.6 ng/in^2 <3.6 ng/in^2 <3.6 ng/in^2	<3.6 ng/in^2
	TETA	10% Ethanol	2 hours at 100°C	<0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$	<0.01 $\mu g/in^2$
			2 hours at 100°C followed by 40°C for 238 hours	<0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$	<0.01 $\mu g/in^2$
		50% Ethanol	2 hours at 100°C	<0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$	<0.01 $\mu g/in^2$
			2 hours at 100°C followed by 40°C for 238 hours	<0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$ <0.01 $\mu g/in^2$	<0.01 $\mu g/in^2$
	Allyl alcohol	10% Ethanol	2 hours at 100°C	<50 ng/in^2 <50 ng/in^2 <50 ng/in^2	<50 ng/in^2
			2 hours at 100°C followed by 40°C for 238 hours	<50 ng/in^2 <50 ng/in^2 <50 ng/in^2	<50 ng/in^2

Continued, Attachment 5.

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Section F - MIGRATION LEVELS IN FOOD - Continued

Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Control sample extracts were used in the validation studies. Since all of the analytes were non-detected in the sample extracts, replicate control sample extracts were spiked with the detection limit amount of each analyte. The spiked extracts were worked up in the same way as the sample extracts and analyzed. In each case, the spiked analyte was detected.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

The following calculations utilize the residual levels provided in Part II, B, 3, and assume (1) 50 mg paper/in^2 treated with 0.5% FCS, and (2) 100% migration to 10 g food/in^2.

FCS

Migration of oligomers is calculated based on the low-molecular weight fraction of the FCS (<1000 Daltons) containing TETA. The basis for this approach is detailed in FCN No. 314; data supporting the low-molecular weight fraction of the FCS is provided in Attachment 4, Appendix D, of this FCN.

50 mg paper/in^2 x 0.005 mg FCS/mg paper x 0.000374 mg oligomers/mg FCS ÷ 10,000 mg food/in^2 = 9.4 x 10^{-9} mg oligomers/mg food = 9.4 ppb

IMPURITIES

Data that support the residual levels of these impurities in the FCS are included in Attachment 4.

50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] epichlorohydrin/mg FCS ÷ 10,000 mg food/in^2 = [ ] [ ]

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50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] 2,3-DCP/mg FCS ÷ 10,000 mg food/in^2 = [ ] [ ]

000018

50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] perfluorohexyl iodide/mg FCS ÷ 10,000 mg food/in^2 = [ ] perfluorohexyl iodide/mg food = [ ]

50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] mg FCS ÷ 10,000 mg food/in^2 = [ ] [ ]

50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] mg FCS ÷ 10,000 mg food/in^2 = [ ] [ ] mg food = [ ]

50 mg paper/in^2 x 0.005 mg FCS/mg paper x [ ] mg FCS ÷ 10,000 mg food/in^2 = [ ] /mg food = [ ]

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Section G- ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

$$\begin{aligned} EDI &= DC \times 3 \text{ kg food/p/d} \\ &= CF \times \langle M \rangle \times 3 \text{ kg food/p/d} \\ &= CF \times [(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})] \times 3 \text{ kg/p/d} \end{aligned}$$

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

One-half the sensitivity level is used below as the maximum level of migration where a substance was not detected at a given sensitivity, and where the chromatography supports the use of one-half the detection limit. In addition, all migration values in µg/in^2 and ng/in^2 were converted to µg/kg food (ppb) as follows: µg/in^2 ÷ 0.01 kg food/in^2 = µg/kg; ng/in^2 ÷ 10 kg food/in^2 = µg/kg.

A consumption factor (CF) of 5% for specialty paper and the food type distribution factors for uncoated paper (59% aqueous, 41% fatty) are used below to calculate the EDI for each substance.

1,3-DCP	(0.13 ppb (µg/kg) x 0.59) + (0.29 ppb x 0.41) x 0.05 CF = 0.0098 ppb 0.0098 µg/kg x 3 kg food/person/day = 0.03 µg/p/d
3-CPD	0.36 ppb (µg/kg) x 0.05 CF = 0.018 ppb 0.018 µg/kg x 3 kg food/person/day = 0.054 µg/p/d
TETA	1 ppb (µg/kg) x 0.05 CF = 0.05 ppb 0.05 µg/kg x 3 kg food/person/day = 0.15 µg/p/d
Allyl alcohol	5 ppb (µg/kg) x 0.05 CF = 0.25 ppb 0.25 µg/kg x 3 kg food/person/day = 0.75 µg/p/d
[redacted]	10 ppb (µg/kg) x 0.05 CF = 0.5 ppb 0.5 µg/kg x 3 kg food/person/day = 1.5 µg/p/d CONFIDENTIAL

The remaining dietary exposure calculations are based on 100% migration calculations provided in Section F(2) above.

Oligomers	9.4 ppb (µg/kg) x 0.05 CF = 0.47 ppb 0.47 µg/kg x 3 kg food/person/day = 1.41 µg/p/d
Epichlorohydrin	[redacted] (µg/kg) x 0.05 CF = [redacted] [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d
2,3-DCP	[redacted] (µg/kg) x 0.05 CF = [redacted] [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d
Perfluorohexyl iodide	[redacted] (µg/kg) x 0.05 CF = [redacted] [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d
[redacted]	[redacted] (µg/kg) x 0.05 CF = [redacted] ppb [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d
[redacted]	[redacted] (µg/kg) x 0.05 CF = [redacted] [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d
[redacted]	[redacted] (µg/kg) x 0.05 CF = [redacted] [redacted] µg/kg x 3 kg food/person/day = [redacted] µg/p/d

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2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: November 15, 2005

From: Division of Food Contact Notifications, Chemistry Review Group 1

Subject: **FCN 542**: Hercules Inc. through Keller and Heckman. Use of 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard. Submissions dated July 26, 2005 (initial submission) and September 8, 2005 (response to deficiencies).

To: Division of Food Contact Notifications, Regulatory Group 1
Attention: P. Honigfort, Ph.D.

Keller and Heckman (K&H) on behalf of Hercules Inc. submitted this food contact notification (FCN) for use of the food contact substance (FCS) identified as 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard (internal sizing application). The FCS, identified as PPD D-1101, will be used at a level not to exceed 0.5% by weight of the dry paper and paperboard intended to contact all food types (I-IX), under conditions of use B-H, as described in Tables 1 and 2, respectively, of 21 CFR 176.170(c) (Components of paper and paperboard in contact with aqueous and fatty foods).

Regulatory Status

The FCS is not currently regulated in 21 CFR 170-199, nor is it the subject of any effective FCNs. The FCS and use limitations are similar to the FCS described in FCNs 314[1] (effective 4/23/03), [redacted] 487[2] (effective 7/14/05) and 518[3] (effective 8/23/05), all submitted by Hercules Inc.

1) FCN 314 was submitted for use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine (aka PPD D-1085) as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard.

[redacted]

3) FCN 487 outlined a new synthetic method for the FCS in FCN 314, identified new impurities and new residual levels for previously known impurities, and expanded the use of the FCS to include size press applications.

[1] Chemistry memorandum for FCN 314 dated March 17, 2003 (S. Elyashiv-Barad to V. Gilliam).
[2] Chemistry memoranda for FCN 487 dated April 26, 2005 (K. Arvidson to P. Honigfort), June 10, 2005 (K. Arvidson to P. Honigfort) and July 6, 2005 (K. Arvidson to File).
[3] Chemistry memorandum for FNC 518 dated September 23, 2005 (K. Arvidson to V. Gilliam).

4) FCN 518 further modified the manufacturing process described in FCN 487, and expanded the use to include microwave susceptors.

Identity

Information on the identity of the FCS is contained in FDA Form 3480, Section II.A, Section II.C, and Attachments 1 and 2 of the initial submission, and Item 1 in the September 8, 2005 submission.

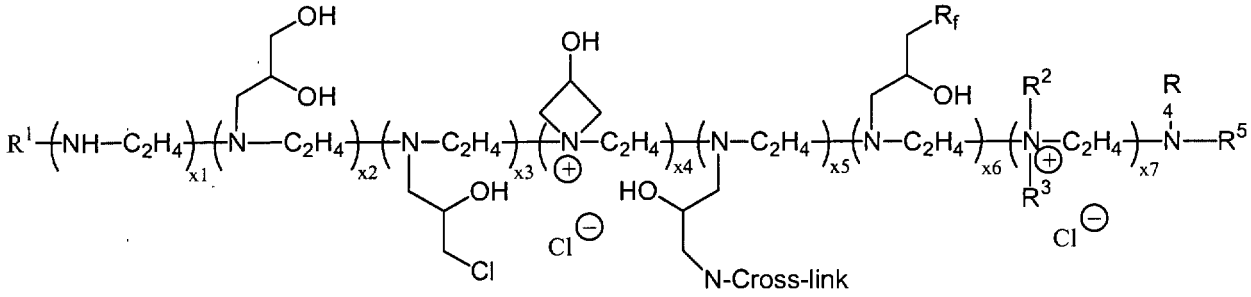
The subject FCS differs from the FCS in FCNs 314, 487 and 518 in the perfluoroalkyliodide component used to manufacture the FCS. The subject FCS uses perfluorohexyl iodide (C6 alkyl) in the manufacture, whereas that in FCNs 314, 487 and 518 uses . The FCS basically consists of a triethylenetetramine (TETA) backbone onto which are substituted groups derived from allyl alcohol (AA), epichlorohydrin (ECH) and perfluorohexyl iodide (PFHI).

CAS Name: 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

CAS Reg. No.: 464178-94-7

Other name: PPD D-1101

Chemical Structure: (Attachment 1 of the FCN)



R^1-R^5 = H; $CH_2CH(OH)CH_2OH$; $CH_2CH(OH)CH_2Cl$; $CH_2CH(OH)CH_2$(N-Cross-link) $CH_2CH(OH)CH_2R_f$

R_f = $F(CF_2)_6$

X_1-X_7 can be in any order (aka random substitution on the TETA backbone).

Molar ratios of (Item 1 of the September 8, 2005 submission).

Molecular weight:

Chemical/Physical Information

Specifications were provided in Section II.C of Form 3480 and reference Hercules test methods used in FCN 314. The notifier provided maximum, minimum and 2 individual batch values for each property reported. An aqueous solution of the polymer has a pH in the range of and a viscosity in the range of The total solids weight- % (wt.-%) is in the range of

The fraction of polymer with a molecular weight below 1000 Daltons is 2.5% (Attachment 4, Appendix C). A discussion on the low molecular weight portion of the FCS (i.e. with a molecular weight less than 1000 Daltons) is provided in the **Migrant Levels in Food** section below.

FCS Characterization

Structural data identifying the FCS is included in Attachment 2 of the initial submission. The notifier provided a proton nuclear magnetic resonance (^{1}H NMR) spectrum that is consistent with the structure of the subject FCS.

We have no questions on the identity of the FCS.

Manufacture

Information concerning the manufacture of the FCS is described in Form 3480, Section II.B, and Attachments 3 and 4 of the initial submission. Raw materials used in the manufacture of the FCS are tabulated in Section II.B, and summarized below. Specifications for the raw materials, with the exception of perfluorohexyl iodide, are provided in Attachment 5 of FCN 314.

Table 1: Raw materials used in the manufacture of the FCS

Chemical	CAS No.	Function
Perfluorohexyl iodide (PFHI)	355-43-1	Starting material
Allyl alcohol (AA)	107-18-6	Starting material
Triethylenetetramine (TETA)	112-24-3	Starting material
Epichlorohydrin (ECH)	106-89-8	Starting material

The manufacturing process is described in Attachment 3 (of the initial submission) and provided below.

Impurities

Information on impurities in the FCS is contained in Form 3480, Section II.B.3 of the initial submission. Typical residual levels of each impurity are included in Section B.3; however, supporting data, such as analytical methods and raw data including standard solutions and corresponding calibration curves, were only provided for PFHI, .

ECH, 2,3-dichloro-1-propanol (2,3-DCP) and . (Appendices B and E of Attachment 4).

In your August 25, 2005 letter, you informed the notifier that residual levels were used to calculate exposure to several of the impurities in this FCN. However, this impurity information appears to be obtained from only one manufactured batch (of unknown composition) of the FCS. You indicated that the notifier should provide the composition (i.e. molar ratio) of the test sample and also discuss why the reported residual levels from this single batch would be representative of the average or typical residual levels for the FCS.

In response to your letter, the notifier indicated that although the specific molar equivalents of the test samples used for the residual analysis (and migration studies) were not determined analytically, they are not expected to differ significantly from the ratio provided for the FCS. To demonstrate the representative nature of the test sample, the notifier provided specific information on the mole equivalents used to produce the sample (see Item 2 in the September 8, 2005 submission), and concluded that because they were within the ranges specified in the manufacturing process, the residual levels measured in this sample may be considered as typical for this FCS. We concur with the notifier's conclusions. The supporting information provided by the notifier is sufficient since exposure (see **Exposure** section below) to these impurities will be based on the assumption of 100% migration to food and not on actual migration results. Impurities and their residual levels (typical), as taken from Section II.B.3, are tabulated below.

Table 2: Impurities in the FCS

Impurity	Function	CAS Reg. #	Typical residual (dry basis, mg/kg)
PFHI	Starting material	355-43-1	
AA	Starting material	107-18-6	
ECH	Crosslinking agent	106-89-8	
1,3-Dichloro-1-propanol (1,3-DCP)	Byproduct of ECH	96-23-1	
2,3-Dichloro-1-propanol (2,3-DCP)	Byproduct of ECH	616-23-9	
3-Chloro-1,2-propanediol (3-CPD)*	Byproduct of ECH	96-24-2	
TETA	Starting material	112-24-3	

* Hydrolysis product of 1,3-DCP.

We have no questions on the manufacture of the FCS.

Intended Use and Technical Effect

Information concerning the intended use and technical effect of the FCS is discussed in Form 3480, Section II.D, of the initial submission, the September 8, 2005 submission (Item 3), and Attachment 6 of FCN 314.

The notifier intends to use the FCS as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard (internal sizing application). The maximum use level of the FCS will not exceed 0.5% by weight of the dry paper and paperboard intended for use in contact with all food types (I-IX) under conditions of use B-H, as described in Tables 1 and 2 of 21 CFR 176.170(c), respectively. The use of this FCS is substitutional for the use of the FCS in FCN 314. Although not explicitly discussed by the notifier, it is our understanding that the subject FCS is thought to be advantageous in that its manufacture uses a homologue that will not result in residual perfluorooctanoic acid (PFOA).

Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water. The notifier notes that data demonstrating the technical effect of a very similar FCS are provided in Attachment 6 to FCN 314. This data was previously reviewed and found to be adequate.[1]

The suggested notification language was provided in Attachment 6 and is not consistent with the proposed use of the FCS. In your August 25, 2005 letter, you informed the notifier that the FCN does not specifically state where the FCS will be applied during the manufacture of paper and paperboard (i.e. wet-end or size-press application). However, both the residue and migration testing data presented in the FCN were obtained from samples where the FCS was applied prior to the sheet-forming operation in the papermaking process. As such, this data would only support the application of the FCS at the wet-end of the papermaking process. For this reason FDA suggested that the notification language include the "wet-end" application of the FCS. In response to your letter, the notifier agreed with this limitation (see Item 3 in the September 8, 2005 submission).

We have no questions about the intended and technical effect of the FCS.

Stability

Information on the stability of the FCS is provided in Form 3480, Section II.E, of the initial submission.

The FCS is reported to be stable under the intended use conditions of B-H (<100°C). Given that the FCS is a polymer and the stability of the related FCS in the aforementioned FCNs, we concur.

We have no questions regarding the stability of the FCS.

Migration Levels in Food

Studies to estimate migrant levels in food were briefly described in Form 3480, Section II.F, and Attachment 5, with the full reports contained in Attachment 4 (initial submission), and summarized below. Attachment 4 (Items I through IV plus Appendices) includes a summary of the primary migration study conducted by Hercules (Item II), a summary of the impurity profile for the FCS (Item III), a determination of LMWOs in the FCS (Item IV), and Appendices: A (analytical methods for the primary migration study),[4] B (analytical methods for product analysis), C (size exclusion chromatography, SEC, data), D (NMR data for LMWO analysis), E (impurity profile raw data), and F (migration study raw data in Parts 1 through 4). An additional migration study for TETA (by Exygen) is contained in Part 4 of Appendix F.

Migration Studies for 1,3-DCP, 3-CPD, [redacted] AA and TETA

Test Samples and Protocol

Migration studies were performed (in triplicate) on paper sheets (basis weight 52.4 mg paper/in^2). Internally treated (containing 0.5 wt-% of the FCS) and untreated (control) sheets were immersed in 10% ethanol (as a non-fatty food simulant) and corn oil (as a fatty food simulant) for analyses of 1,3-DCP, 3-CPD and [redacted] and in 10% ethanol and 50% ethanol (as a fatty food simulant) for analyses of TETA. We note that for AA, studies were only carried out in 10% ethanol.

Treated and untreated (control) sheets (2.5" x 2.5" pieces, 20 pieces for each individual extraction, 120 in^2 total one-sided surface area exposed) were separated by screens and placed in two-sided extraction cells (capable of withstanding high pressure) along with the food simulant (240 mL), giving a food simulant-to-surface area ratio of 2 mL/in^2 paper.[5] (The notifier notes that no precipitation was observed in the extracts after the extraction period using this ratio.) The samples were extracted (in triplicate) using the protocol for condition of use B (2 hr at 100°C followed by 238 hr at 40°C). Extracts were analyzed at 2 and 240 hr (a total of 6 extractions for each food simulant). Analytical methods used by the notifier are described in Appendices A (for the analysis of 1,3-DCP, 3-CPD, [redacted] and AA) and F (for the analysis of TETA) of Attachment 4, and are summarized below.

Analysis

[redacted] As noted above, the extracts were analyzed at 2 and 240 hrs for 1,3-DCP, 3-CPD, [redacted], AA and TETA.

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[4] In Appendix A, the notifier provided analytical reports for 1) the determination of ECH, 1,3-DCP, 2,3-DCP, and 3-CPD in paper extracts using 10% ethanol and corn oil, 2) the determination of [redacted] using 10% ethanol and corn oil), and 3) the determination of AA using 10% ethanol and 50% ethanol. We note that the notifier provided a description of the determination of ECH and 2,3-DCP, but not the actual migration results for these migrants. Nonetheless, as discussed below, exposure to these 2 impurities was based on residual levels and the assumption of 100% migration to food.

[5] In the case of AA, the notifier did not provide a detailed description of the test protocol. In the case of TETA: 20 2" x 2" square pieces separated by metal screens. Total food simulant 200 mL. Total surface of paper exposed 80 in^2.

1.3-DCP and 3-CPD.

Standard solutions of 1,3-DCP and 3-CPD in 10% ethanol (0.5, 2.5, 10, 25, and 50 ng/mL) were prepared by serial dilution of a stock solution of ECH, 1,3-DCP, 2,3-DCP and 3-CPD in ethyl acetate. Standard solutions of 1,3-DCP and 3-CPD in corn oil (2.5, 5, 10, 25, and 50 ng/mL) were prepared by serial dilution of a stock solution of ECH, 1,3-DCP, 2,3-DCP and 3-CPD in acetonitrile. Calibration curves in 10% ethanol and corn oil were provided in Appendix F of Attachment 4.

The 10% ethanol extracts were analyzed directly for

Standard solutions of in 10% ethanol (0.00252, 0.063328, 0.12666, and 0.63328 µg/mL) and corn oil (0.02647, 0.05445, 0.07506, and 0.09555 µg/mL) were prepared by serial dilution of a stock solution of in acetonitrile. Calibration curves in 10% ethanol and corn oil were provided in Appendix F of Attachment 4.

AA.

Four standard solutions of AA in 10% ethanol (0.0108, 0.0502, 0.1076 and 0.3587 ng/mL) were prepared by serial dilution of an AA stock solution. Calibration curves in 10% ethanol were provided in Appendix F of Attachment 4.

TETA.

Standard solutions of TETA in 10% and 50% ethanol (2.5, 5.0, 10, 25, 50 and 100 ng/mL) were prepared by serial dilution of a TETA stock solution with 10% and 50% ethanol, respectively. The stock solution was prepared by addition of water to TETA (reported as 80% pure). The solutions were analyzed by Calibration curves were provided in Appendix F of Attachment 4.

Additional Analytes. The notifier did not analyze the extracts for migration of [redacted] ECH, 2,3-DCP or [redacted] We did not request migration data for these analytes since exposure will be based on 100% migration to food and not on actual migration results (see **Exposure** below).

Migration Results

Test conditions and corresponding migration values (average for each time period) for internally treated sheets (containing 0.5 wt-% FCS), as taken from Form 3480, Section II.F, and Attachments 4 and 5 (initial submission) are summarized below with our modifications (see footnotes to Table 3).

Table 3: Average migration results for internally treated sheets (0.5 wt.-% FCS)

Food simulant / Migrant	Migration (10% ethanol)		Migration (corn oil or 50% ethanol)	
	2 hr/100°C (ng/in^2)	240 hr/40°C (ng/in^2)	2 hr/100°C (ng/in^2)	240 hr/40°C (ng/in^2)
1,3-DCP	<1.3	<1.3	<2.9	<2.9
3-CPD	<3.6	<3.6	<3.6	<3.6
[redacted]	<100	<100	<100	<100
AA	<100[a]	<100[a]	---	---
TETA	<10	<10	<10[b]	<10[b]

[a] We applied a factor of 2 to the migration values to account for poor recovery of AA.
[b] Due to analytical difficulties in the analysis of TETA in corn oil, 50% ethanol was used as the fatty-food simulant.

As is evident from Table 3 above, all the analytes were reported by the notifier as "non-detect" in the food simulants. As discussed in more detail below in relation to Table 4, the notifier's "non-detect" level on some analytes actually corresponded to the lowest standard concentration (LSC). Inspection of the supporting chromatograms indicated that some migrants gave detectable peaks at the reported level, while other migrants did not. For example, the 2 and 240 h extract chromatograms for 1,3-DCP and 3-CPD in corn oil were very flat with no distinguishable peaks. For AA, the value in Table 3 is 2 times the notifier's reported "non-detect" value to account for the poor recovery in 10% ethanol (see discussion below).

Validation

Spiking and recovery studies were conducted (in triplicate) on all control extracts prior to sample work-up. The 2 hour control extracts were used in the case of 3-CPD and 1,3-DCP, while the 2 and 240 hour control extracts were used in the case of TETA. In the case of [redacted] and AA, it is unclear from the submission which control extracts, *i.e.*, the 2 hour or 240 hour, were spiked. As all analytes were generally not detected, the control samples were spiked at the reported "non-detect" level in each food simulant and, thus, recoveries were generally not determined.

The notifier provided raw data, representative chromatograms and calibration curves in Appendix F of Attachment 4 (initial submission). We summarized the validation data provided by the notifier in Table 4, below, and calculated recoveries.

Table 4: Summary of the validation data contained in Appendix F of Attachment 4 (initial submission)

Migrant	Food simulant	Standard solutions		Fortification (ng/mL, ng/in^2)	Average Recovery (%)
		used for migration studies	used for validation studies		
1,3-DCP	10% Ethanol (ng/mL)	0.5, 2.5, 10, 25, 50	0.5, 2.5, 5, 10, 25, 50	<0.65, <1.3	119
	Corn Oil (ng/mL)	2.5, 5, 10, 25, 50	0.5, 2.5, 10, 25, 50	<1.5, <2.9	33
3-CPD	10% Ethanol (ng/mL)	0.5, 2.5, 10, 25, 50	0.5, 2.5, 5, 10, 25, 50	<1.8, <3.6	100
	Corn Oil (ng/mL)	2.5, 5, 10, 25, 50	Same	<1.8, <3.6	94
[redacted]	10% Ethanol (μg/mL)	0.00252, 0.063328, 0.12666, 0.63328	Same	<50, <100	61
	Corn Oil (μg/mL)	0, 0.02647, 0.05445, 0.07506, 0.09555	0.02647, 0.05445, 0.07506, 0.09555	<50, <100	76
AA	10% Ethanol (ng/mL)	0.0108, 0.0502, 0.1076, 0.3587	Same	<25, <50	31
TETA	10% Ethanol (ng/mL)	2.5, 5, 10, 25, 50, 100	Same	<4, <10	155
	50% Ethanol (ng/mL)	2.5, 5, 10, 25, 50, 100	Same	<4, <10	96

Inspection of Table 4 (columns 4 and 5) indicates that in a number of cases, the notifier's "non-detect" level is actually the LSC and not a limit of detection (LOD) for the analytical method. Thus, spiking the extracts at the LSC would be expected to give acceptable recoveries, while spiking at an LOD would not. Furthermore, inspection of Table 3 in Attachment 4 (item 2) and Table 4 above indicates that with the exception of AA (10% ethanol) and 1,3-DCP (corn oil), the reported (or calculated) recoveries are acceptable. In the case of 1,3-DCP in corn oil, the control sample was fortified at a level that is *slightly above* the LSC reported for the migration studies. On the other hand, 1,3-DCP was not detected on visual inspection of the chromatograms, in fact the

chromatograms were reasonably flat. We will use the notifier's reported migration value for 1,3-DCP in corn oil. In the case of AA, we applied a correction factor to compensate for the low average recovery of AA in 10% ethanol.

Low-Molecular-Weight (LMW) Oligomers Containing TETA

The notifier did not analyze the test extracts described above for LMW oligomers. Rather, migration of LMW oligomers, *i.e.* specifically the fraction having a molecular weight <1000 Daltons, was based on the wt.-% fraction present in the FCS and the assumption of 100% migration to food (see below).

Size exclusion chromatography (SEC) indicated that 2.5 wt.-% of the dry weight of the FCS consisted of LMW oligomers <1000 Daltons, with about 2.4 wt.-% being <500 Daltons. The LMW oligomer fraction was further analyzed by ^{1}H NMR to determine the proportion of TETA-related oligomers. The notifier notes that this technique has been previously described and validated in FCN 314. The level of LMW oligomers containing TETA was found to be 14,800 μg/g LMW oligomer (ppm based on the total solids weight, or 1.5 wt.-%) using equation 1 in Appendix D. Therefore, the LMW fraction composed solely of TETA-containing oligomers is 374 μg/g FCS (2.5% x 14,800 μg/g). A description of the analytical methods and corresponding spectra were provided in Appendices C and D of Attachment 4).

In the approach described above, the notifier determined that ~1.5% of the LMW fraction is composed of TETA-containing oligomers. While this may seem to be an artificially low level, the remaining fraction of LMW oligomers (>98%) would contain fluorinated species *not* on a TETA backbone. Exposure to the these fluorinated containing-LMW oligomers would be accounted for in the exposure estimates to other fluorinated impurities, such as [redacted], determined below.

We have no questions about the studies used to determine migrant levels in food.

Consumer Exposure

Exposure estimates can be found in FDA Form 3480, Section II.F, of the initial submission. Exposure estimates for LMW oligomers containing TETA and 6 impurities (PFHI, [redacted], ECH, 2,3-DCP and [redacted]) were determined assuming 100% migration to food while those for 5 impurities (1,3-DCP, 3-CPD, [redacted], AA and TETA) were determined using migration results. The exposure estimates are presented below.

LMW oligomers containing TETA

The notifier calculated the dietary concentration (DC) of LMW oligomers containing TETA using the previously discussed SEC data and the assumption of 100% migration to food based on the following assumptions:

1. 100% migration of the LMW oligomers to food.
2. LMW oligomers <1000 Dalton and containing TETA are present in the FCS at a level of 374 mg oligomer/kg FCS.
3. The maximum level of the FCS in paper is 0.5 g FCS/100 g paper.
4. A paper basis weight of 50 mg paper/in^2 paper.[6]
5. A food mass-to-surface area ratio of 10 g food/in^2 paper.

The concentration of the TETA-containing LMW oligomers in food (<M>) was calculated as follows:

$$\left(\frac{374x10^{-6}\ g\ oligomers}{g\ FCS}\right)\left(\frac{0.5\ g\ FCS}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{in^2\ paper}\right)\left(\frac{in^2\ paper}{10\ g\ food}\right) = 9.4x10^{-9}\ \frac{g\ oligomer}{g\ food} = 9.4\ ppb$$

Using the <M> (calculated above) and a consumption factor (CF) of 0.05 for specialty treated paper,[7] the DC of the FCS is:

DC_{FCS} = CF x <M> = 0.05 x 9.4 ppb = 0.47 μg/kg or 0.47 ppb

The estimated daily intake (EDI), based on a daily diet of 3 kg food/person/day, is:

EDI_{FCS} = 3 kg food/p/d x 0.47 μg FCS/kg food = 1.4 μg FCS/p/d

We concur with the notifier's exposure estimates for the FCS (as TETA containing-LMW oligomers).

Residual Impurities

1,3-DCP, 3-CPD, [redacted] *AA and TETA*

We calculated exposure to these impurities based on the migration results (modified as in Table 3), the paper and paperboard food-type distribution factors ($f_{aqueous + acidic} = 0.59$, $f_{alcohol + fatty} = 0.41$), and a CF of 0.05. The DC and EDI of 1,3-DCP is calculated below:

[6] In a memorandum of meeting dated April 13, 1995 (A. Bailey), it was determined that the average basis weight of paper for these types of calculations would be 50 mg/in^2. This conclusion was supported by the observation that food-contact paper and paperboard basis weights range from 20-100 mg/in^2.

[7] A CF of 0.05 is representative of specialty paper. See the chemistry memorandum for FCN 255 dated September 4, 2002 (effective September 5, 2002; A. Bailey to H. Macon) and the chemistry memorandum for FCN 59 dated August 1, 2000 (effective August 16, 2000; R. Costantino to E. Machuga).

$$DC_{1,3\text{-DCP}} = CF \times [(f_{aqueous + acidic} \times M_{10\% \text{ Ethanol}}) + (f_{alcohol + fatty} \times M_{\text{Corn oil}})]$$

$$= 0.05\ [(0.59 \times <0.13 \text{ ppb}) + (0.41 \times <0.29 \text{ ppb})] = <10 \text{ ng/kg} \quad \text{or} \quad <10 \text{ pptr}$$

$$EDI_{1,3\text{-DCP}} = <10 \text{ ng 1,3-DCP/kg food} \times 3 \text{ kg food/p/d} = <30 \text{ ng 1,3-DCP/p/d}$$

Similarly, the DCs and EDIs for 3-CPD, [redacted], AA and TETA were calculated and tabulated below.

Table 5: Exposure estimates based on actual migration results

Impurity	Migration* (µg/kg or ppb)	DC	EDI
1,3-DCP	<0.13 (10% ethanol) <0.29 (corn oil)	<10 pptr	<30 ng/p/d
3-CPD	<0.36 (10% ethanol) <0.36 (corn oil)	<18 pptr	<54 ng/p/d
[redacted]	<10 (10% ethanol) <10 (10% corn oil)	<0.5 ppb	<1.5 µg/p/d
AA	<10 (10% ethanol)	<0.5 ppb	<1.5 µg/p/d
TETA	<1 (10% ethanol) <1 (50% ethanol)	<0.05 ppb	<0.15 µg/p/d

* From Table 3, above.

The DCs reported by the notifier are not significantly different from those values we report in this memorandum, with the exception of AA. In the case of AA, our exposure estimate is twice that reported by the notifier.

PFHI, [redacted] ECH, 2,3-DCP and [redacted]

The notifier did not analyze the test extracts for these impurities. Nonetheless, the notifier reported DCs using the reported residual levels and assuming 100% migration to food as was the case for the LMW oligomers containing TETA.

We employed a different approach to model the internal addition of a non-substantive paper additive to paper. This is referred to as our "wet-end" model[8] in the FCN/FAP guidance document. This model is also acceptable for water-soluble impurities in an FCS or a food additive. In the present case, while these impurities may not necessarily have a high water solubility, we would expect them to have significant water solubility given their low residual levels in the FCS (see Table 2, above). The following assumptions are made in our "wet-end" model:

[8] For a more detailed description of the "wet end" model see the chemistry memorandum for FAP 5B4472 dated April 16, 1996, A. Bailey to D. Harrison, and the chemistry memorandum for FAP 3B4367 dated April 30, 1999, A. Bailey to V. Gilliam.

1. The substance is not substantive to paper.
2. Additives are typically introduced into the papermaking process at the headbox,[9,10] which contains a whitewater slurry consisting of about 0.6 weight % pulp.[11,12]
3. Prior to entering the dryers, the whitewater slurry (containing the additive) is concentrated to contain approximately 33% pulp and 67% water. Since the additive is not substantive to paper, the mass of water (containing the additive) in contact with pulp at the point in the papermaking process where the slurry enters the dryers, determines the level of additive retained in the paper.
4. Any substance present after sheet forming remains in the finished paper on steam drying.
5. Finished paper contains approximately 92% pulp and 8% water.
6. The basis weight of paper is 50 mg/in^2.[10]
7. 100% migration of the FCS from the finished paper to food.
8. A food mass-to-surface area ratio of 10 g food/in^2 paper.
9. A CF of 0.05.

As an example, the DC of PFHI is calculated below. The residual level (typical) of PFHI in the FCS (see Table 2, above) is 308 mg/kg, and the FCS is added at the "wet end" at a maximum of 0.5% by weight/g paper. The PFHI in the water slurry is found to be:

$$\left(\frac{308x10^{-6}\ g\ PFHI}{g\ FCS}\right)\left(\frac{0.5\ g\ FCS}{100\ g\ paper}\right)\left(\frac{100\ g\ paper}{92\ g\ fiber}\right)\left(\frac{0.6\ g\ fiber}{100\ g\ slurry}\right)=1.0x10^{-8}\ g\ PFHI/g\ slurry$$

The concentration of PFHI in the finished paper is then calculated.

$$\left(\frac{1.0x10^{-8}\ g\ PFHI}{g\ slurry}\right)\left(\frac{67\ g\ slurry}{33\ g\ fiber}\right)\left(\frac{92\ g\ fiber}{100\ g\ paper}\right)\left(\frac{0.05\ g\ paper}{in^2\ paper}\right)\left(\frac{in^2\ paper}{10\ g\ food}\right)=$$

$$=9.4x10^{-11}\ g\ PFHI/g\ food$$

---

[9] Casey, J.P., *Pulp and Paper Chemistry and Technology, Volume 2: Papermaking*, 2nd ed., New York: Interscience Publishers, Inc., 1960, pp. 947 and 1013-1014.

[10] The headbox is a pressurized flowbox that distributes paper stock onto the Fourdrinier wire, an endless screen belt that enhances drainage, as the paper sheets are formed. See Smook, G., *Handbook for Pulp and Paper Technologists*, Joint Executive Committee of the Vocational Education Committee of the Pulp and Paper Industry, 1992, p.208.

[11] See, for example, Calkin, J.B. and J.L. Parsons in *Modern Pulp and Paper Making*, ed. J.B. Calkin, 3rd ed., New York: Reinhold, 1957, Ch. 11, p. 312.

[12] White water is a general term for water removed from a pulp slurry and containing fiber fines and additives. On the paper machine, white water is the water that flows through the Fourdrinier as the paper sheets are formed. White water is frequently recycled in the papermaking process. The terms "white water" and "process water" are interchangeable. See Smook, G., *Handbook for Pulp and Paper Technologists*, Joint Executive Committee of the Vocational Education Committee of the Pulp and Paper Industry, 1992, pp. 227, 395.

The DC and EDI of PFHI from the proposed use of the FCS is:

DC_{PFHI} = CF x <M> = 0.05 x 94 ng PFHI /kg food = 4.7 ng/kg or 4.7 pptr

EDI_{PFHI} = 4.7 ng PFHI/kg food x 3 kg food/p/d = 14 ng/p/d

Similarly, exposures to [redacted] ECH, 2,3-DCP and [redacted] were calculated and tabulated below.

Table 6: Exposure estimates based on our "wet-end" model

Substance	Typical residual* (dry basis, mg/kg)	<M> (ng/kg or pptr)	DC wet-end model (ng/kg or pptr)	EDI (ng/p/d)
PFHI	[redacted]			
[redacted]				
ECH				
2,3-DCP				
[redacted]				

* From Table 2, above.

[redacted]

The DC of [redacted] using our "wet-end" model and a residual level of [redacted] (see Table 2, above) was determined to be [redacted] (or pptr), corresponding to an EDI of [redacted]

[redacted]

PFOA

As discussed above, it is our understanding that the subject FCS is thought to be advantageous in that its manufacture uses a homologue that will not result in residual perfluorooctanoic acid (PFOA).

Risk Assessments

Upper-bound risk estimates for ECH, 2,3-DCP, 3-CPD and 1,3-DCP from the proposed use of the FCS were calculated by the notifier. We recalculated upper bound risks for the 4 impurities by multiplying our EDI (in mg/kg-bw/d) by the carcinogenic unit risk [in $(mg/kg\text{-}bw/d)^{-1}$]. The results are tabulated below.

Table 7: Upper-bound risk estimates

Substance	Unit risk* $(mg/kg\text{-}bw/d)^{-1}$	EDI (mg/kg-bw/d)	Upper-bound unit risk
ECH	0.0027		
2,3-DCP	0.034		
3-CPD	0.0109	$8.3x10^{-8}$	$9x10^{-9}$
1,3-DCP	0.034	$5x10^{-7}$	$2x10^{-8}$
* Unit risk values as found in our database (ECH) or in the February 10, 2000 memorandum from the Division of Heath and Human Effects Evaluation (2,3-DCP, 3-CPD and 1,3-DCP). Upper-bound risks rounded to 1 SF.			

Notification Language

The acknowledgment letter, as signed off by Chemistry on September 15, 2005, is appropriate as written.

Conclusion

We have no questions on this FCN. As noted in the **Regulatory Status section**, FCN 487 expanded the use of the FCS in FCN 314 to include size press applications. In was brought to our attention that in similar cases we have actually recommended that the notifier combine these applications, i.e., the "wet-end" and size press applications, into one FCN. The use is FCN 487 subsumes the use in FCN 314 and thus, the description of FCN 314 in our Inventory of Effective FCNs (http://www.cfsan.fda.gov/~dms/opa-fcn.html) could read "replaced by FCN 487", rather than "Effective".

Sharon Elyashiv-Barad, Ph.D.

SOLENIS FCN 746

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II A 1 through 4

1 Chemical Abstracts Service (CAS) name

2-Propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2 CAS Registry Number

464178-94-7

3 Trade or Common Name

PPD D-37614, imPress FP200

4 Other Chemical Names *(IUPAC, etc)*

5 Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s) For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n For new copolymers, also provide the ratio of monomer units in the copolymer

See **Attachment 1** for chemical structure. The chemical formula is as follows:

(See **Attachment 2** for supporting molecular weight data)

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6 Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

NMR data are provided in FCN No. 542, Attachment 2.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II A 4 a through d

1 List all reagents monomers, solvents, catalyst systems, purification aids, etc used to manufacture the FCS Include chemical name, CAS Reg No , and function in the manufacture of the FCS

CONFIDENTIAL

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
		CONFIDENTIAL	☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II B 3 If no support this conclusion in the manufacturing process description (#2)

2 Describe the manufacturing process, including reaction conditions (e g , times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions Describe any purification steps

The manufacturing process is included in **Attachment 3**

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SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II A 4 a through d

List impurities in the FCS including the chemical names, CAS Reg Nos , and typical and maximum residual levels (percent weight) in the FCS as it will be marketed For FCSs that are polymers, include typical and maximum residual monomer concentrations Provide supporting data including analytical methods and validation information

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (ppm)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
				☒ Yes ☐ No
			CONFIDENTIAL	☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
			CONFIDENTIAL	☒ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II G of this form If no, provide an explanation below

*See **Attachment 3** for additional information regarding these residual levels.

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SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II A 5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications Values, provide minimum or maximum specification limits or a range, as appropriate

For the FCS:

SPECIFICATION	VALUE

6. For polymeric FCSs provide the following additional information

6 Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity Analytical methods should be included Where appropriate, provide test results for at least three production batches of the FCS

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
pH (Hercules IM 443-4 Method)	6.3	3.5	4 54, 3.91, 4.43
Wt% total solids (Hercules IM 443-2 Method)	15	10	12.68, 14 81, 10.8
Brookfield viscosity (cps, 25°C) (Hercules IM 443-3 method)	300	N/A	4 0, 263, 4.5

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

(1) Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods

Weight percent polymer below 1000 Daltons = ----

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Weight percent polymer below 500 Daltons = ----

(See **Attachment 2** for further information regarding the molecular weight profile)

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SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II B and II C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended. ☒ Single Use ☐ Repeat Use

The FCS is intended for use an oil/grease resistant sizing agent in the manufacture of paper and paperboard, employed either prior to the sheet forming operation or at the size press, at levels up to 0.75% by weight of the dry paper and paperboard intended for use in contact with food.

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2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
FCS in paper and paperboard up to 0.75% by weight of the dry paper and paperboard.	All food types (Types I - IX)	A through H

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2 a CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b For repeat-use articles, provide a typical use scenario Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article

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3 State the intended technical effect of the FCS Summarize data demonstrating that the FCS will achieve the intended technical effect Specifically address the minimum amount required to achieve the intended technical effect Include data as an attachment

Oil/grease/fat and water stains can weaken paper, making it susceptible to punctures and tears. In addition, the stains hurt the print quality of the paper and can make the bag appearance undesirable to the consumer. When the oil/grease/fat or water contained in the paper bag/container wets the outer surface of the bag/container, the surfaces the paper comes in contact with can become slippery, creating a safety hazard. Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water.

Data demonstrating the technical effect of a substance very similar to the FCS are provided in Attachment 6 to FCN No. 314. (The only difference between the FCSs covered by FCN No. 314 and the present FCS is [redacted]); thus, the technical effect data are equally applicable to this FCS)

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The minimum amount needed to achieve the intended technical effect is 0 05%- 0.75%.

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SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II D 2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS If no degradation is expected, so state

None.

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Part II - CHEMISTRY INFORMATION

2 List the breakdown products for the FCS and provide CAS names, CAS Reg Nos , and structures, as appropriate Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II G of this form

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

STRUCTURE	STRUCTURE

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

STRUCTURE	STRUCTURE

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc) must be attached

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II D 5)*, skip to Section II F 2 and provide full details of all calculations

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II D 1 through II D 3

a. Describe test specimen(s), including full composition (e.g , comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e g , density, T_g, T_m, % crystallinity) Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Approximately 50 mg/in^2 (50 lb/3000 ft^2) paper samples containing 0.75% FCS applied as a surface treatment to the paper were used in the migration studies Paper sheets prepared without the FCS were used as controls The samples and controls were extracted by total immersion

Due to analytical difficulties encountered when corn oil was used as the extractant, 50% ethanol in water was used in the analysis of TETA

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b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e g , 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2) If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e g , turbidity or precipitation data) showing that saturation of the food simulant has not occurred

The samples and controls were extracted with 10% ethanol-in-water to simulate contact with aqueous, acidic, and low alcohol ($\leq$ 15% by volume alcohol) foods To simulate contact with fatty foods, 50% ethanol or corn oil was used. A two-sided extraction cell was used for all testing. A 2 ml/in^2 simulant volume to surface area ratio, counting the area of one side of the samples, was used.

The samples and controls were exposed to the food simulants at Condition of Use A test conditions, that is, 121°C for 2 hours followed by 10 days at 40°C. No precipitation was noted in the resulting extracts under these conditions.

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
50 lb/3000 ft² uncoated paper sheets treated at 0.75% dry weight FCS	1,3-DCP	10% Ethanol	2 hours at 121°C	<5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
		Corn oil	2 hours at 121°C	<5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
	3-CPD	10% Ethanol	2 hours at 121°C	30 ng/in² 4.8 ng/in² 22 ng/in²	19 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
		Corn oil	2 hours at 121°C	5 ng/in² <5 ng/in² <5 ng/in²	<5 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<5 ng/in² 7.7 ng/in² 6.9 ng/in²	7.3 ng/in²
	TETA	10% Ethanol	2 hours at 121°C	<6.3 ng/in² <6.3 ng/in² <6.3 ng/in²	<6.3 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<6.3 ng/in² <6.3 ng/in² <6.3 ng/in²	<6.3 ng/in²
		50% Ethanol	2 hours at 121°C	<6.3 ng/in² <6.3 ng/in² <6.3 ng/in²	<6.3 ng/in²
			2 hours at 121°C followed by 40°C for 238 hours	<6.3 ng/in² <6.3 ng/in² <6.3 ng/in²	<6.3 ng/in²

d Provide a summary of method validation results Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels Full details, including description of spiking procedure and calculations, must be included as an attachment

Spiked amounts were determined by the level of analyte found in the extracts With analyte levels of 3-CPD detected close to the detection limit, spiked amounts at 1x, 2x, and 4x the detection limit were added to control samples. If the analytes were not detected, control samples were spiked with the detection limit amount of each analyte. The spiked extracts were worked up in the same way as the sample extracts and analyzed. In each case, the spiked analytes were detected.

Analyte	10% Ethanol in Water		Corn Oil	
	Amount Added to Control (ng/in^2) (spiked amount)	% Recovery	Amount Added to Control (ng/in^2) (spiked amount)	% Recovery
1,3-DCP	5.0	Detected	5.0	87
3-CPD	5.0	99	5.0	132
	10	86	10	109
	20	78	20	90
TETA	6.3	Detected	6.3	Detected

The relative standard deviation (% RSD) for the % Recovery for 3-CPD was 10% for 10% ethanol in water extracts and 17% for corn oil extracts

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2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II D for discussions on 100% migration calculations, II D 4 for information on FDA's migration database, and II D 5 for migration modeling

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS Fully describe assumptions made in deriving the estimates and show all calculations

Migration of the FCS to food has been calculated on a worst-case basis. Details of these calculations are set forth in **Attachment 4.**

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II E and Appendix IV

e EDI for the notified use must be calculated by the notifier for both the FCS and any migrants The notifier is also responsible for providing nulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS The notifier may wish to consult FDA obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)* If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached The following general equation is used to calculate an EDI

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See **Attachment 5** for EDI calculations

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2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II F 2 and the use scenario information described in Section II D 2 b, show the calculations used for determining DC and EDI for the FCS and any migrants

Not Applicable

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate Provide cumulative EDI (CEDI) to include this use, where appropriate

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Oligomers	Not Listed	9 4	0.47	0.00141	
Epichlorohydrin	106-89-8	--			
2,3-DCP	616-23-9				
--					CONFIDENTIAL
1,3-DCP	96-23-1	0.25	0.017	0 000051	
3-CPD	96-24-2	1.39	0.07	0.00021	
TETA	112-24-3	0.63	0.032	0 000096	
Allyl Alcohol	107-18-6	--			
				CONFIDENTIAL	

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Memorandum

Date: September 12, 2007

From: Division of Food Contact Notifications, Chemistry Review Group 1

Subject: **FCN 746**: Hercules Inc. through Keller and Heckman. Expanded use of 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation (internal sizing) and/or at the size press (external sizing) in the manufacture of paper and paperboard. Submissions received June 6, 2007 (initial submission), July 2, 2007 (clarification regarding the proposed use) and September 12, 2007 (clarification on calculations involving low molecular weight oligomer fraction).

To: Division of Food Contact Notifications, Regulatory Group 2
Attention: V. Komolprasert, Ph.D.

Keller and Heckman (K&H) on behalf of Hercules Inc. (Hercules) submitted this food contact notification (FCN) to expand the use of the food contact substance (FCS) identified as 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation (internal sizing) and/or in the size press (external sizing) in the manufacture of paper and paperboard.

The FCS will be used at a level not to exceed 0.75% by weight (wt.-%) of dry paper and paperboard intended to contact all foods under Conditions of Use A-H as described on our website. The FCN also outlines an improved synthetic method intended to reduce the impurity levels in the FCS. The FCS, referred to as imPress FP200 and PPD D-37614 in the FCN, is marketed as an aqueous solution containing 10-15 weight-percent (wt.-%) solids.

Regulatory Status

The FCS is not currently regulated in 21 CFR 170-199. Hercules's FCN 542[1] (effective November 25, 2005) is for use of the FCS, identified as PPD D-1101, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation (internal sizing) in the manufacture of paper and paperboard, at a level not to exceed 0.5 wt.-% of the dry paper and paperboard, intended to contact all foods under Conditions of Use B-H.

In comparison to FCN 542, the subject FCN serves to introduce an improved manufacturing method, include addition at the size press, increase the use level from 0.5 wt.-% to 0.75 wt.-%, and include Conditions of Use A.

[1] Chemistry memorandum for FCN 542 dated November 15, 2005 (S. Elyashiv-Barad to P. Honigfort).

The FCS is similar to the FCSs described in Hercules's FCNs 314[2] (effective April 23, 2003), 467[3] [4]

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1) FCN 314 was submitted for use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine (aka PPD D-1085) as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard. The FCS may be used at a level not to exceed 0.5 wt.-% of dry paper and paperboard in contact with all food under Conditions of Use B-H.
2) FCN 467 was submitted to expand the use of the FCS in FCN 314 to include use as a grease-proofing agent in microwave heat-susceptor packaging. FCN 467 was withdrawn due to deficiencies.
3) FCN 487 outlined a new synthetic method for the FCS in FCN 314, identified new impurities and new residual levels for previously known impurities, and expanded the use of the FCS to include size press applications (external sizing). The FCS may be used at a level not to exceed 0.5 wt.-% of dry paper and paperboard in contact with all food under Conditions of Use B-H.
4) FCN 518 further modified the manufacturing process described in FCN 487, and expanded the use to include microwave heat-susceptor packaging.

Although the identity of the FCS in FCNs 542 and the subject FCN is different than that in FCNs 314 and 487, the only differences in the use limitations are the use levels (0.75 wt.-% vs 0.5 wt.-%) and conditions of use (A-H vs B-H).

Chemistry information is contained in FDA Form 3480, Attachments 1 (chemical structure), 2 (molecular weight distribution, MWD), 3 (manufacturing description and impurity levels), 4 (migration calculations), 5 (exposure calculations), 6 (migration study and identity of the low molecular weight oligomers), and incorporated by reference from FCNs 542 and 314. The notifier provided the suggested language in Attachment 7, with modifications provided in the July 2, 2007 e-mail.

Identity

Information on the identity of the FCS is contained in FDA Form 3480, Sections II.A and II.C, and Attachments 1 and 2. *This information was previously reviewed and accepted in FCN 542 and is summarized below for convenience*.

As indicated in the November 15, 2005 chemistry memorandum for FCN 542, the FCS basically

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[2] Chemistry memorandum for FCN 314 dated March 17, 2003 (S. Elyashiv-Barad to V. Gilliam).
[3] Chemistry memoranda for FCN 487 dated April 26, 2005 (K. Arvidson to P. Honigfort), June 10, 2005 (K. Arvidson to P. Honigfort) and July 6, 2005 (K. Arvidson to the File).
[4] Chemistry memorandum for FNC 518 dated September 23, 2005 (K. Arvidson to V. Gilliam).

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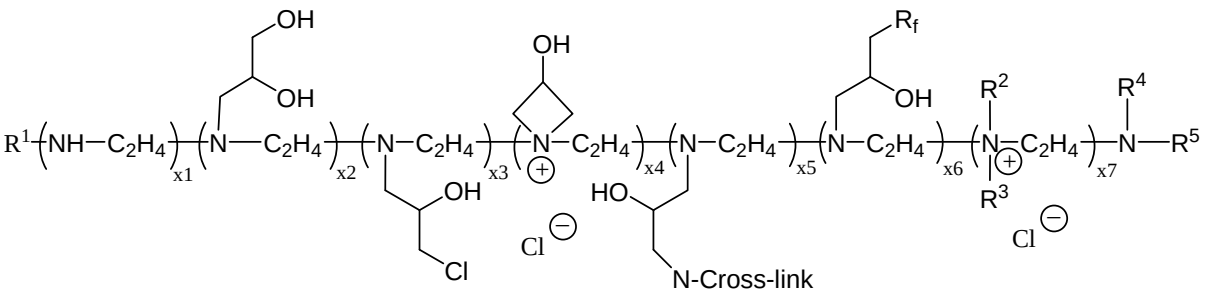
CAS Name: 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

CAS Reg. No.: 464178-94-7

Other names: PPD D-37614; imPress FP200

Chemical Structure: (Attachment 1 of the FCN)



R^1-R^5 = H;
$CH_2CH(OH)CH_2OH$;
$CH_2CH(OH)CH_2Cl$;
$CH_2CH(OH)CH_2$(N-Cross-link)
$CH_2CH(OH)CH_2R_f$ where $R_f = (CF_2)_5CF_3$

X_1-X_7 can be in any order (aka random substitution on the TETA backbone)

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Molecular weight distribution (MWD)

The weight-average (Mw) and number-average (Mn) molecular weights were reported as -- -- and -- -- Daltons, respectively (see Attachment 2 of the subject FCN), based on the size exclusion chromatography (SEC) data contained in FCN 542 (Appendix C). That information is identical to that contained in Attachment 6 (Appendix A) of the subject FCN.

As discussed in our November 15, 2005 memorandum on FCN 542, SEC indicated that -- -- of the dry weight of the FCS consisted of low molecular weight oligomers (LMWOs) <1000 Daltons, with about -- -- being <500 Daltons. As described in Attachments 2 and 6 (see Section IV) of the subject FCN, this value was refined to -- -- by accounting for the presence of residual TETA (154 µg/g "dry", see Table 2 below). This is described in more detail in the **Migrant Levels**

in Food section, below[5].

Specifications/Properties

Specifications for the FCS (pH, viscosity and wt-% total solids) are provided in Section II.C. The pH and viscosity specifications are similar to those reported in FCN 542. The range of total solids reported in the subject FCN (10-15 wt-%) is *lower* than that reported in FCN 542 (16-18 wt-%).

Characterization

The notifier referenced Attachment 2 of FCN 542 which contains a proton nuclear magnetic resonance (^{1}H NMR) spectrum that is consistent with the structure of the subject FCS.

We have no questions on the identity of the FCS.

Manufacture

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5 As described below, the value of - - --

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Impurities

Information on impurities in the FCS, including typical residual levels, as taken from Form 3480, Section II.B.3 and Attachments 3[6] and 6 (see Section II and Appendix C), is shown in Table 2 below. The impurity levels below are based on the analysis of the FCS containing 14.81 wt.-% total solids. We note that impurities in the FCS, -- -- are identical to those identified in FCN 542 (see Table 2). -- -- -- --

The notifier provided adequate supporting data, including the analytical methods and raw data, for all impurities in Attachment 6: Appendices C (-- -- -- --, AA, ECH, 1,3-DCP, 2,3-DCP, 3-CPD, and -- -- D (TETA) and G -- -- With the exception of TETA and -- -- these methods were review and accepted in our review of FCN 542. The methods and results for TETA and PFOA are summarized below.

TETA. Appendix D of Attachment 6 contains a report on analysis of 3 liquid formulations of the FCS for TETA. The testing was conducted by Exygen Research in State College, PA. The samples, identified as X33648-38, X33258-40-1 and X33258-41-1, were reported to contain about 15 wt.-% solids. Samples of each (0.022 g) were placed in PP centrifuge tubes, 2% formic acid added (10 mL), and the contents vortexed and sonicated. Aliquots (2 mL) from each were loaded onto a FluroFlash SPE cartridge and eluted with 2% formic acid (2 mL) and then 0.5% formic acid in 60:40 acetonitrile:water (6 mL). The final volume was reported to be 50 mL. Aliquots were taken for TETA analysis by LC/MS/MS using a gradient (0.1% formic acid/water to 0.1% formic acid/50:50 acetonitrile:water). Each sample was tested in triplicate.

Calibration standards were prepared at concentration of 2.5, 5.0, 10, 25, 50 and 100 ng/mL (ppb) TETA in methanol by serial dilution of a stock solution of TETA in methanol. Supporting data on calibration standards, including a calibration curve, is contained in the Appendix.

Average TETA levels in the liquid samples were as follows: X33648-38 (42.4 ppm), X33258-40-1 (17.2 pm) and X33258-41-1 (22.8 ppm). Accounting for the reported solids levels on X33258-40-1 (15.35%) and X33258-41-1 (14.81%), these values correspond to "dry" levels of 112 ppm (X33258-40-1) and 154 ppm (X33258-41-1).

Spiking of the test samples (in triplicate) was conducted prior to workup, with spiking levels of 5, 10 and 25 ng/mL, and treated as described above. Average recoveries were in the range of 75-122%. Supporting data on validation studies is contained in the Appendix.

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6 The residual levels (dry) for 1,3-DCP and 3-CPD in D-1101 were reported as 5300 ppm and 3500 ppm, respectively, in Attachment 3. The origin of these values is not clear. As reflected in Table 2 of this memorandum, lower values were reported in our November 15, 2005 memorandum on FCN 542.
7 Samples IDs were taken from Table 1 in the Appendix.

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Typical levels of impurities (dry basis) are summarized in Table 2 for convenience as taken from Attachment 3 (with the exception of 1,3-DCP and 3-CPD which were taken from our November 15, 2005 memorandum on FCN 542. We believe that the values in Attachment 3 are in error).

Table 2: Typical Levels of Impurities in the FCS (Compared to that in FCN 542)

Impurity	**CAS#**	**FCN 746 (dry basis, mg/kg)**	**FCN 542 (dry basis, mg/kg)**
- - --		- - --	

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AA ECH	107-18-6 106-89-8	--	3900 <30
1,3-Dichloro-1-propanol (1,3-DCP)[a]	96-23-1	1180	991
2,3-Dichloro-1-propanol (2,3-DCP)[a]	616-23-9	--	3.6
3-Chloro-1,2-propanediol (3-CPD)[b]	96-24-2	293	653
--			
Hydrolysis product of ECH.[b] Hydrolysis product of 1,3-DCP.			
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We have no questions on the manufacture of and impurities in the FCS.

Intended Use and Technical Effect

Information concerning the intended use and technical effect of the FCS is discussed in Form 3480, Section II.D, and further clarified in the July 2, 2007 e-mail.

The FCS is intended for use as an oil/grease-resistant sizing agent for food contact paper and paperboard, at levels not to exceed 0.75% by weight of the dry paper, in contact with all foods under Conditions of Use A-H as described on our website. Use of the subject FCS (manufactured by Hercules from PFHI and the subject of FCNs 542 and 746) would "substitute" for the use and FCS (manufactured by Hercules from a mixture of perfluoroakyl iodides and the subject of FCNs 314 and 487). Moreover, the FCS and use would also "substitute" for similar greaseproofing agents and uses that are permitted for use in contact with food.

Paper treated with the FCS becomes more resistant to staining/penetration by oil/grease/fat and water. The notifier noted that data demonstrating the technical effect of a very similar FCS were provided in Attachment 6 to FCN 314. This data was previously reviewed and found to be adequate[2] and used to support the technical effect (external sizing agent) of the FCS in FCN 487.

According to the Hercules website,[8] the imPress™ ST line of products are cellulose reactive, surface sizing agents designed to impart high levels of sizing for a variety of applications. These products

8 http://ppd.herc.com/innovations/impress™_sizing_and_printability_technology_.asp

are reported to be low foaming, are compatible with most size press additives, and enable the paper manufacturer to change the balance between wet-end (internal) and surface (external) size addition.

In your June 28, 2007 e-mail to Ms. Langhorn of K&H, you indicated that in the Form 3480, Part II.D (intended use), the FCS will be employed either prior to the sheet forming operation (internal sizing) or at the size press (external sizing) in the manufacture of paper and paperboard, suggesting that the FCS can be used in only one of the two paper processing operations and not both. However, there may be situations where a paper manufacturer may add the FCS in at both step in the papermaking process, as long as the total level of the FCS does not exceed 0.75 wt.-% of finished dry paper and paperboard. Therefore, you recommended that the language for the intended use be broaden such that the FCS can be used prior to the sheet forming operation and/or at the size press in the manufacture of paper and paperboard. The notifier's July 2, 2007 e-mail indicated that they concur with the revision of the intended use language for this FCS.

We have no questions about the intended use and technical effect of the FCS.

Stability

Information on the stability of the FCS is provided in Form 3480, Section II.E.

The FCS is reported to be stable under the intended use conditions of A through H. Given that the FCS is a polymer and the stability of the related FCS in the aforementioned FCNs, we concur.

We have no questions regarding the stability of the FCS.

Migrant Levels in Food

Studies to estimate migrant levels in food were briefly described in Form 3480, Section II.F, and the full report is contained in Attachment 6. Attachment 6 (Items I- IV plus Appendices A-G) includes a summary of the impurity profile for the FCS (Item II), summary of the migration studies conducted by Hercules and Exygen (Item III), determination of LMWOs in the FCS (Item IV), and Appendices: A (size exclusion chromatography data), B (NMR data for LMWO analysis), C, D, G (impurities), and E and F (migration study raw data).

On the whole, the migration studies described below are similar to those submitted in support of FCN 542 and previously reviewed and accepted by FDA.

LMWOs containing TETA (<1000 Daltons)

In Attachment 4, the notifier calculated a weight-average (<M>) migration to food of 9.4 µg/kg (ppb) for LMWOs containing TETA (<1000 Daltons) using the previously discussed SEC data and the assumption of 100% migration as described in the November 15, 2005 memorandum on FCN 542. The proportion of LMWOs containing TETA (<1000 Daltons) was determined to be 14,800

µg/g (~1.5 wt.-%)[9] of the LMWO fraction obtained from SEC when analyzed by ^{1}H NMR. Therefore, LMWO containing TETA (<1000 Daltons) was determined to be 374 µg/g FCS (2.5% x 14,800 µg/g).

In the subject FCN, this value was further refined to account for the presence of residual TETA in the FCS (154 µg/g "dry"). Using a dry sample weight of 0.0032 g (from Attachment 6, Appendix D, "wet" weight of 0.022 g and based on 14.81% solids) the absolute amount of TETA would be 0.5 µg (154 µg/g x 0.0032 g). This value (0.5 µg) would equate to 123 µg/g based on the dry weight of the isolated fraction (0.004 g) used in the ^{1}H NMR analysis (from Attachment 6, Appendix B). Subtracting this value from the total weight of 374 µg/g for all component gives a value of 251 µg/g for LMWOs containing TETA (<1000 Daltons). This value was used by the notifier to estimate exposure. In an email dated September 11, 2007 to K&H, you requested clarification on these calculations.

In an email response dated September 12, 2007, K&H agreed with our suggestion that the aforementioned value of 374 µg/g for LMWO containing TETA (<1000 Daltons) can be further refined to account for TETA monomer by simply subtracting the residual level of TETA in the FCS (154 µg/g "dry", maximum). Rather than use 154 µg/g, we used a value of 133 µg/g which was an average of the two reported values as described above (112 µg/g and 154 µg/g). Thus, the refined value is 241 µg/g (374 µg/g - 133 µg/g). We will use this value to estimate exposure to LMWO containing TETA units (<1000 Daltons).

Migration Studies for 1,3-DCP, 3-CPD and TETA

Test Samples and Protocol

Migration studies were performed (in triplicate) on paper sheets (basis weight of 50 lbs/ft^2 or 50 mg paper/in^2) that were externally surface-treated (0.75 wt-% of PPD D-37614) and untreated (as control). Test sample and control sheets were immersed in 10% ethanol (as a non-fatty food simulant) and corn oil (as a fatty food simulant) for analyses of 1,3-DCP and 3-CPD and in 10% ethanol and 50% ethanol (as a fatty food simulant) for analyses of TETA.

Treated and untreated (control) sheets (2.5" x 2.5" pieces, 20 pieces for each individual extraction, 120 in^2 total one-sided surface area exposed) were separated by screens and placed in two-sided extraction cells (capable of withstanding high pressure) along with the food simulant (240 mL), giving a food simulant-to-surface area ratio of 2 mL/in^2 paper. (The notifier notes that no precipitation was observed in the extracts after the extraction period using this ratio.) The samples were extracted (in triplicate) using the protocol for condition of use A (2 hr at 121ºC followed by 238 hr at 40ºC). Extracts were collected at 2, 24, 96 and 240 hr with analysis conducted at all time points (1,3-DCP and 3-CPD) or 2 and 240 hr (TETA). Analytical methods used by the notifier are

9 As noted in our November 15, 2005 memorandum on FCN 542, the notifier determined that ~1.5% of the LMW fraction is composed of TETA-containing oligomers. While this may seem to be an artificially low level, the remaining fraction of LMWO (>98%) would contain fluorinated species *not* on a TETA backbone. Exposure to the these fluorinated containing-LMWO would be accounted for in the exposure estimates to other fluorinated impurities, such as C6 iodohydrin, C6 epoxide and C6 alcohol.

described at the end of Appendices E (1,3-DCP and 3-CPD) and F (TETA) of Attachment 6, and are summarized below.

Analysis
Sample extracts were analyzed by gas chromatography (GC) equipped with a halogen-specific (XSD) detector or a micro-electron capture detector (ecd), with the exception of TETA which was analyzed by liquid chromatography with tandem mass spectrometry (LC/MS/MS).

1,3-DCP and 3-CPD. The 10% ethanol extracts (10 mL aliquot) were transferred to glass vessels, evaporated (to remove ethanol), sodium chloride (0.5 g) and water (0.5 mL) added and the aqueous phase absorbed onto an Extrelut SPE column (which retains the polymer and water), followed by elution with ethyl acetate (20-30 mL) and concentration by evaporation under nitrogen. The residue was diluted to 2.0 mL with ethyl acetate. The corn oil extracts (24 mL) were partitioned into acetonitrile (10 mL) , washed with hexane (50 mL) and the aqueous phase diluted to 10.0 mL with acetonitrile. All extracts were analyzed by GC-XSD.

Standard solutions of 1,3-DCP and 3-CPD in 10% ethanol (0.5, 2.5, 10, 25, and 50 ng/mL) were prepared by serial dilution of a stock solution of 1,3-DCP and 3-CPD in ethyl acetate. Standard solutions of 1,3-DCP and 3-CPD in corn oil (2.5, 5, 10, 25, and 50 ng/mL) were prepared by serial dilution of a stock solution of 1,3-DCP and 3-CPD in acetonitrile. The standard solutions were analyzed by GC-XSD. Calibration curves in 10% ethanol and corn oil were provided in Appendix E of Attachment 6.

The limit of detection (LOD) for both analytes in the simulants was reported as 5 ng/in^2. Taking into account the dilution factors (24 for 10% ethanol, 12 for corn oil) and final volumes (2 mL for 10% ethanol, 10 mL for corn oil), this value corresponds to <12 ng/mL for the 10% ethanol extracts and <5 ng/mL for the corn oil extracts (see the equations in Appendix E). Thus, the notifier's LODs for each simulant actually fall in the range of the calibration standards. Actual LODs would be expected to be lower than those reported by the notifier.

TETA. Aliquots (1 mL) of the 10% and 50% ethanol extracts (2, 24 and 96 h) were transferred to polypropylene (PP) containers and refrigerated. At the end of 240 h, the entire extract was transferred to PP containers and refrigerated. The extracts contained no visually observable contamination, and thus, no filtering was required. Samples of the 2 and 240 h aliquots were then transferred to a PP autosampler vial and analyzed by LC/MS/MS.

Standard solutions of TETA in 10% and 50% ethanol (2.5, 5.0, 10, 25, 50 and 100 ng/mL) were prepared by serial dilution of a TETA stock solution with 10% and 50% ethanol, respectively. The stock solution was prepared by addition of water to TETA (reported as 80% pure). The solutions were analyzed by LC/MS/MS. Calibration curves were provided in Appendix F of Attachment 6.

The LOD was reported as 2.5 ng/mL for both simulants. Given that there was no sample concentration, this corresponds to 5 ng/in^2 (2.5 ng/mL x 2 mL/in^2).

Additional Analytes. The notifier did *not* analyze the extracts for migration of other analytes.

Expposure to these substances will be based on 100% migration to food and not on actual migration results.

Migration Results
Test conditions and corresponding migration values for each analyte (corrected for controls and averaged for each time period) are summarized below as taken from Form 3480, Section II.F, and Attachment 6 (see Section III.b of Attachment 6).

Table 3: Summary of Migration Values

Migrant	**10% Ethanol (ng/in^2)**				**Corn oil or 50% ethanol (ng/in^2)**			
	2 h	**24 h**	**96 h**	**240 h**	**2 h**	**24 h**	**96 h**	**240 h**
1,3-DCP	<5	<5	<5	<5	<5	<5	<5	<5
3-CPD	19	15	<5	<5	<5	<5	<5	7.3
TETA	<6.3	N/A	N/A	<6.3	<6.3	N/A	N/A	<6.3

As is evident from Table 3, 1,3-DCP and TETA were reported as "non-detect" in the food simulants. As noted above, the notifier's "non-detect" levels actually correspond to the lowest standard concentration or another concentration on the calibration curve. Inspection of the supporting chromatograms indicated that some migrants gave detectable peaks at the reported level, while other migrants did not. For example, the 2 and 240 h extract chromatograms for 1,3-DCP in 10% ethanol and 1,3-DCP and 3-CPD in corn oil were very flat with no distinguishable peaks. It is likely that "true" LODs would be lower than the "non-detect" levels used by the notifier.

Validation
Spiking and recovery studies were conducted (in triplicate) on all control extracts prior to sample work-up (see Section II.F of Form 3480). In the case of 1,3-DCP and 3-CPD, the time period for the control extracts was not identified and the spiking levels were 5, 10 and 20 ng/in^2. As shown in Section II.c of Attachment 6, 1,3-DCP was detected while recoveries for 3-CPD ranged from 80-130%. In the case of TETA, the 240 hour control extracts were used and TETA was detected.

We have no questions about the studies used to determine migrant levels in food.

Consumer Exposure

Information on exposure estimates for the FCS and other migrants is summarized in Form 3480, Section II.G.3, and supporting information is contained in Attachments 4 and 5. Exposure estimates for LMWOs containing TETA (<1000 Daltons) and 9 impurities [redacted] were determined assuming 100% migration to food while those for 3 impurities (1,3-DCP, 3-CPD and TETA) were determined using migration results. The exposure estimates are presented below.

LMWOs containing TETA (<1000 Daltons)

As discussed in Attachment 5, the notifier calculated a dietary concentration (DC) of 0.47 ppb for LMWOs containing TETA (<1000 Daltons) using the same approach as outlined for FCN 542. In

fact, the DC in FCN 542 was also 0.47 ppb (see our November 15, 2005 memorandum on FCN 542). The *higher* use level (0.75 wt.% vs 0.5 wt.-%) and *lower* value for LMWO containing TETA (<1000 Daltons) (251 µg/g vs 374 µg/g) resulted in the same values for the DC.

Given that the notifier has refined the value for LMWO containing TETA units (<1000 Daltons), we can refine the DC of 0.47 ppb. Multiplying the DC by a factor of 0.96 derived from the ratio of the "refined use levels" (241/251= 0.96) gives a DC of 0.45 ppb. This value is not significantly different that that reported by the notifier.

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As discussed in Attachment 4, the notifier calculated DCs for these 9 impurities (they did not include -- -- using the reported residual levels and assuming 100% migration to food as was the case for the LMWOs containing TETA (<1000 Daltons).

As discussed in our November 15, 2005 memorandum on FCN 542, we employed our "wet-end" model to estimate impurity levels in paper based on the internal addition of a non-substantive paper additive to paper. This model is acceptable for water-soluble impurities. While the impurities associated with the present FCS may not necessarily have high water solubility, we would expect them to have significant water solubility given their low residual levels in the FCS. This approach would also apply for the subject FCN.

The DCs for FCN 542 are shown in Table 4 (below). The DCs for the 9 impurities in the subject FCN -- -- were simply "extrapolated" from the ratios of the impurity and use levels. For example, in FCN 542 a DC

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1,3-DCP, 3-CPD and TETA

As discussed in Attachment 5, the notifier calculated exposure to these impurities based on the migration results expressed as migration to food, the food-type distribution factors for paper and paperboard ($f_{aqueous+acidic}$ = 0.59, $f_{alcohol+fatty}$= 0.41) and a consumption factor (CF) of 0.05. The notifer used one-half their reported LOD for migration of 1,3-DCP into 10% ethanol but not for corn oil. We used one-half the notifier's LOD for "non-detected" migration and the values in Table 3. We calculated DCs as follows:

$DC_{1,3\text{-DCP}}$ = CF x [($f_{aqueous + acidic}$ x $M_{10\% Ethanol}$) + ($f_{alcohol + fatty}$ x $M_{Corn oil}$)]
= 0.05 [(1)(½ x <5 ng/in^2 x 1 in^2/10 g food)]
= <0.013 ng/g or <0.013 µg/kg or <0.013 ppb

$DC_{3\text{-CPD}}$ = CF x [($f_{aqueous + acidic}$ x $M_{10\% Ethanol}$) + ($f_{alcohol + fatty}$ x $M_{Corn oil}$)]
= 0.05 [(0.59)(19 ng/in^2 x 1 in^2/10 g food) + (0.41)(7.3 ng/in^2 x 1 in^2/10 g food)]
= 0.05 [(0.59)(1.9 ng/g) + (0.41)(0.73 ng/g)]
= 0.07 ng/g or 0.07 ppb

DC_{TETA} = 0.05 [(1)(½ x <6.3 ng/in^2 x 1 in^2/10 g food)]
= <0.015 ng/g or <0.015 µg/kg or <0.015 ppb

The DCs reported by the notifier based on migration studies are not significantly different from those values in this memorandum.

Summary of Exposure Estimates

The DC for LMWOs containing TETA units (<1000 Daltons) is 0.45 ppb, a DC value not significantly different than that determined in our November 15, 2005 memorandum on FCN 542. This was the result of a *higher* use level (0.75 wt.% vs 0.5 wt.-%) and *lower* value for LMWOs containing TETA <1000 Daltons (220 µg/g vs 374 µg/g).

With regard to the impurity DC values as summarized in Table 5, - - --

- - --

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Table 5: Summary of Typical Levels (from Table 2) and DCs for Impurities

Substance	FCN 542 (0.5 wt.-%)		FCN 746 (0.75 wt.-%)	
	Level (dry, mg/kg)	DC (ng/kg or pptr)	Level (dry, mg/kg)	DC (ng/kg or pptr)
--		--		
AA	3900	<500[b]	--	
ECH	<30	0.46[a]	--	
1,3-DCP	991	<10[b]	1180	<13[f]
2,3-DCP	3.6	0.06[a]	1.2	0.03[e]
3-CPD	653	<18[b]	293	70[f]
TETA	NA[d]	<50[b]	154	<15[f]
--		--		

a-based on "wet-end" model in FCN 542; b- based on migration studies in FCN 542;
c- error in November 15, 2005 memorandum corrected as discussed in the text; d- not addressed in FCN 542, estimated at 0.1 ng/kg as discussed in the text; e-determined as described in the text; f-based on migration studies in FCN 746.

Comments on Cumulative Exposure

As noted above, use of the subject FCS (manufactured by Hercules from --and the subject of FCNs 542 and 746) would "substitute" for the use and FCS (manufactured by Hercules from a mixture of perfluoroakyl iodides and the subject of FCNs 314 and 487). Moreover, the FCS and use would also "substitute" for similar greaseproofing agents and uses that are permitted for use in contact with food. In order to provide comments on cumulative exposure to the FCS and impurities, we have turned to the memoranda on the related FCS and use in FCN 487. The language in our April 26, 2005 memorandum on FCN 487 is shown below in italics:

Oligomers

As stated above, the exposure to the oligomers is expected to be no greater than that calculated in FCN 314. Since the use of the FCS as described in this notification is substitutional for the use described in FCN 314, the CEDI for the oligomers of the FCS will remain at 1.5 μg/p/d.

Impurities

In FCN 314, exposures to allyl alcohol, the fluorotelomer iodides, fluorinated iodides, fluorinated epoxides, epichlorohydrine, and 2,3-DCP were estimated using our wet-end paper model, which provided very small exposures to these compounds. As described in FCN 487, the FCS is applied to paper as a coating at the size press, which results in higher exposures to these impurities. Although the use of the FCS described in FCN 487 is substitutional, exposures to these impurities, as

calculated above, are worst-case estimates and would subsume those provided in FCN 314. Exposures to the fluorinated alcohol byproducts, 1,3-DCP, 3-CPD, and TETA, as calculated above, should also be considered worst-case estimates for the use of the FCS as a paper additive.

Using this approach for the FCS that is the subject of FCNs 542 and 746, we conclude that a DC of 0.45 ppb for LMWOs containing TETA units (<1000 Daltons) would represent both FCNs 542 and 746. The *highest* DC value for each individual impurity (as shown in Table 5, above) would represent cumulative exposure for each impurity for both FCN 542 and 746. As for common impurities that are found in the FCS in FCNs 314/487 and that in FCNs 542/746, the *highest* DC value for each would represent cumulative exposure for each impurity (as shown in this memorandum and the April 26, 2005 memorandum on FCN 487). This conclusion does *not* include use of the FCS in FCNs 312/487 in microwave heat-susceptor applications (FCN 518).

Notification Language

The acknowledgment letter dated July 7, 2007 is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb:8-19-07 (FCN746_C_memo)
RDInit: ABBailey, 9/12/07
Final: abb, 9/12/07

Attachment 4
Migration Calculations for FCS and Impurities

The following calculations utilize the residual levels provided in Part II, Section B-3, and assume (1) a paper basis weight of 50 mg/in^2 (2) a treatment level of 0.75% FCS, and (3) 100% migration to 10 g food/in^2.

Food Contact Substance

Migration of oligomers is calculated based on the low-molecular weight fraction of the FCS (<1000 Daltons) containing TETA. Size-exclusion chromatography (SEC) was used to isolate a <1000 Da fraction (method described in Attachment 2). The SEC fraction was 2.543% of the dry weight of the final product. The isolated fraction was then analyzed by NMR to determine the amount of triethylenetetramine related components contained in the fraction. The absolute level of TETA related components in the low molecular weight SEC fraction was performed using 1H NMR using an internal standard (Attachment 2). The level in the SEC fraction was determined to be 14,800 ppm (ug/g based on the weight of the total solids in the SEC fraction-see Attachment 2).
Therefore the <1000 Da fraction composed of TETA-containing oligomers would be 374 ug/g [2.543% x 14,800 ppm = 374 ppm = 374 ug/g].

The amount of residual TETA in the product was determined to be 154 µg/g (dry weight). Using a dry solids sample weight of 0.0032 g (based on 14.81% solids), the absolute amount of TETA is determined to be 0.49 µg (154 µg/g x 0.0032 g = 0.50 µg). This value would equal 123 µg if the dry weight (0.004 g) of the isolated low molecular weight fraction < 1,000 daltons is used (0.49 µg ÷ 0.004 g = 123 µg/g). Subtracting this value from the total weight of 374 µg/g for all components with a molecular weight below 1,00 daltons gives a dry weight of 251 µg/g for oligomers with a MW < 1,000 daltons (374 µg/g – 123 µg/g = 251 µg/g).

Accordingly, migration of the FCS oligomers is calculated as follows: 50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 251 x 10^{-6} mg oligomers/mg FCS ÷ 10,000 mg food/in^2 = 9.4 x 10^{-9} mg oligomers/mg food = 9.4 ppb

Impurities

Data that support the residual levels of these impurities in the FCS are included in **Attachment 6, Appendices C through G.** Migration of the impurities is calculated using the same assumptions detailed above.

Epichlorohydrin	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x [redacted] epichlorohydrin/mg FCS ÷ 10,000 mg food/in^2 = [redacted]
2,3-DCP	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x [redacted] 2,3-DCP/mg FCS ÷ 10,000 mg food/in^2 = [redacted]
Perfluorohexyl iodide	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 169 x 10^{-6} mg perfluorohexyl iodide/mg FCS ÷ 10,000 mg food/in^2 = 6.3 x 10^{-9} mg perfluorohexyl iodide/mg food = **6.3 ppb**
3-Perfluorohexyl-2-iodopropan-1-ol	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 169 x 10^{-6} mg 3-perfluorohexyl-2-iodopropan-1-ol/mg FCS ÷ 10,000 mg food/in^2 = 6.3 x 10^{-9} mg 3-perfluorohexyl-2-iodopropan-1-ol/mg food = **6.3 ppb**
3-(Perfluoro-n-hexyl)prop-2-enol	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 196 x 10^{-6} mg 3-(perfluoro-n-hexyl)prop-2-enol/mg FCS ÷ 10,000 mg food/in^2 = 7.4 x 10^{-9} mg 3-(perfluoro-n-hexyl)prop-2-enol /mg food = **7.4 ppb**
Tridecafluoroheptyl oxirane	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 169 x 10^{-6} mg tridecafluoroheptyl oxirane/mg FCS ÷ 10,000 mg food/in^2 = 6.3 x 10^{-9} mg tridecafluoroheptyl oxirane/mg food = **6.3 ppb**
PFHA	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 81 x 10^{-6} mg PFHA/mg FCS ÷ 10,000 mg food/in^2 = 2.4 x 10^{-9} mg PFHA/mg food = **3.0 ppb**
PFOA	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x 6.9 x 10^{-7} mg PFOA/mg FCS ÷ 10,000 mg food/in^2 = 2.6 x 10^{-11} mg PFOA/mg food = **0.026 ppb**
Allyl Alcohol	50 mg paper/in^2 x 0.0075 mg FCS/mg paper x [redacted] mg allyl alchohol/mg FCS ÷ 10,000 mg food/in^2 = [redacted]

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Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II A 1 through 4

1 Chemical Abstracts Service (CAS) name

-Propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

2 CAS Registry Number

464178-94-7

3 Trade or Common Name

(b)(4) [redacted]

4 Other Chemical Names *(IUPAC, etc)*

none

5 Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s) For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n For new copolymers, also provide the ratio of monomer units in the copolymer

See **Attachment 1** for chemical structure The chemical formula is as follows

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(b)(4) [redacted]

Confidential

(See **Attachment 5** for supporting molecular weight data)

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

6 Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS

NMR data were provided in FCN No 542, Attachment 2, and are incorporated herein by reference

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II A 4 a through d

List all reagents monomers, solvents, catalyst systems, purification aids, etc used to manufacture the FCS Include chemical name, CAS Reg No , and function in the manufacture of the FCS

CHEMICAL NAME	CAS REG NO	FUNCTION	Is residual expected to remain in the final food contact material?†
(b)(4)			
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II B 3 If no support this conclusion in the manufacturing process description (#2)

2 Describe the manufacturing process, including reaction conditions (e g , times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions Describe any purification steps

The manufacturing process is included in **Attachment 2**

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*

See Chemistry Recommendations, Sections II A 4 a through d

List impurities in the FCS including the chemical names, CAS Reg Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
(b) (4)				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
				☒ Yes ☐ No
(b) (4) Allyl alcohol	107-18-6	(b) (4)		☒ Yes ☐ No
Epichlorohydrin	106-89-8			☒ Yes ☐ No
1,3-Dichloro-2-propanol (1,3-DCP)	96-23-1			☒ Yes ☐ No
2,3-Dichloro-1-propanol (2,3-DCP)	616-23-9			☒ Yes ☐ No
3-Chloro-1,2-propanediol (3-CPD)	96-24-2			☒ Yes ☐ No
Triethylenetetramine (TETA)	112-24-3			☒ Yes ☐ No
(b) (4)				☒ Yes ☐ No
				☒ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II G of this form. If no, provide an explanation below

See **Attachment 5** for additional information regarding impurity levels in FCS

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II A 5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Include specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS

SPECIFICATION	VALUE

For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
(b) (4) [redacted]			

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods

Weight percent of molecular species below 1000 Daltons = (b) (4)

(b) (4)

Weight percent of molecular species below 500 Daltons = (b) (4)

(See **Attachment 5** for further information regarding the calculation of maximum percentage of oligomeric species)

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II B and II C

1 Describe the intended use of the FCS Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable Indicate whether single or repeat use (or both) is intended ☒ Single Use ☐ Repeat Use

The FCS is intended for use as an oil/grease resistant agent in the manufacture of paper and paperboard, employed either prior to the sheet forming operation and/or at the size press, at levels up to 0 75% by weight of the dry paper and paperboard intended for use in microwave heat-susceptor packaging

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2 a For single-use articles, list the food types expected to contact the FCS, with examples if known Refer to the food type classifications in the chemistry recommendations, when possible Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
FCS in paper and paperboard up to 0 75% by weight of the dry paper and paperboard intended for use in microwave heat-susceptor packaging	All food types (Types I - IX)	Condition of Use J (Microwave Susceptor Conditions)

000011

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2 a CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b For repeat-use articles, provide a typical use scenario Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article

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Part II - CHEMISTRY INFORMATION *(continued)*

3 State the intended technical effect of the FCS Summarize data demonstrating that the FCS will achieve the intended technical effect Specifically address the minimum amount required to achieve the intended technical effect Include data as an attachment

(b) (4) [redacted]

Data demonstrating the technical effect of a substance very similar to the FCS are provided in [redacted] (b) (4) 314 (The only difference between the FCSs covered by FCN No 314 and the present FCS is [redacted] (b) (4) thus, the technical effect data included in FCN No 314 are equally applicable to this FCS, and are incorporated herein by reference

(b) (4) [redacted]

The minimum amount needed to achieve the intended technical effect is 0 05%- 0 75%

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SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II D 2

1 Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS If no degradation is expected, so state

To determine the potential weight loss and thermal degradation of the FCS when used in microwave susceptor packaging, a thermal gravimetric analysis (TGA) of the FCS was performed

See **Attachment 5** for reports entitled "*Thermal/Oxidation Stability on ImPress FP 200 Under Dynamic Condition – Simulation of Microwave Popcorn Conditions*" and "*Thermal Gravimetric/Mass Spectrometric Analysis of PPD D-1435 under Oxidative Conditions*" As shown therein, the FCS, when exposed to a heating profile similar to microwave conditions such as a temperature increase from room temperature to 240°C within 3 minutes and 20 seconds under an air atmosphere, experienced weight loss values at 220, 225, 233, and 240°C, of 10 2, 12 3, 16 6, and 20 9 wt %, respectively At 220°C, the temperature associated with microwave cooking of popcorn on a susceptor, approximately 10 2% of the polymer was lost

To identify the degradation products created during heating, thermal gravimetric analysis (TGA) was carried out in a flow through furnace tube at temperatures from room temperature to 240°C at a temperature rise of 55°C/min while approximately 100 ml/minute of air was passed through the tube into a liquid nitrogen cooled collection trap

The D-1435 material collected in the cold trap during TGA was then analyzed by gas chromatography/mass spectroscopy (GC/MS) The mass fragments obtained were consistent with 1H-perfluorohexane (retention time 1 4 min), perfluorohexane (retention time 1 65 min), and 1,3-dichloro-2-propanol (retention time 3 9 min) Substances corresponding to peaks with retention times of 1 5 min and 2 min , present at concentrations much less than 1H-perfluorohexane, perfluorohexane, and 1,3-dichloro-2-propanol, were not identified but contained fragments consistent with perfluoroalkyl -CF_3 groups and are potentially associated with perfluoroalcohols and hydrogen substituted perfluoroalkyl compounds The retention times for these species were all less than 5 minutes under the conditions of the GC/MS analysis

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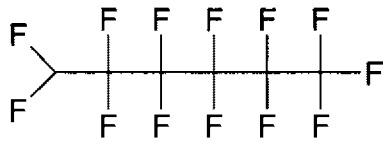
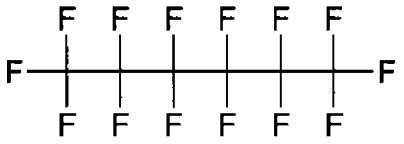
Part II - CHEMISTRY INFORMATION

2 List the breakdown products for the FCS and provide CAS names, CAS Reg Nos , and structures, as appropriate Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II G of this form

1H-perfluorohexane	355-37-3	Perfluorohexane	355-42-0
$H(CF_2)_5CF_3$ 		$F(CF_2)_5CF_3$ 	

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc) must be attached

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II D 5)*, skip to Section II F 2 and provide full details of all calculations

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II D 1 through II D 3

a Describe test specimen(s), including full composition (e g , comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e g , density, T_g, T_m, % crystallinity) Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side

The migration study to determine the potential migration of the FCS made use of paper specimens with a basis weight of 25 lbs/3000 ft^2 (26 mg/in^2) Untreated paper was used as a control and the test samples consisted of the paper treated with 0 75% FCS on a dry weight basis The extracts were analyzed for 1,3-DCP and 3-CPD The control and sample sheets were folded up at the edges to form a "tray" to contain the food simulant Heat susceptors were then glued to the bottoms of the "trays" so that the controls and treated paper were between the heat susceptor and the food simulant

A second migration study was conducted on paper treated with 0 75% FCS The test was carried out as described above and the extracts were examined for the migration of the decomposition products listed in Part II, E 2

The results of these migration studies are included in **Attachment 5**

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b Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e g , 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²) If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e g , turbidity or precipitation data) showing that saturation of the food simulant has not occurred

Corn oil was added to the "trays" and the filled trays containing approximately 5 g oil/in^2 were placed in a 700 watt microwave oven and heated on "high" for 5 minutes

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

Summarize results of migration testing for each test specimen Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below) In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in² For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
25 lb/3000 ft^2 uncoated paper sheets treated at 0 75% dry weight FCS	1,3-DCP	Corn Oil	5 minutes at 700 watts	< 0 012 $\mu g/in^2$ < 0 012 $\mu g/in^2$ < 0 012 $\mu g/in^2$	< 0 012 $\mu g/in^2$
	3-CPD	Corn Oil	5 minutes at 700 watts	< 0 012 $\mu g/in^2$ < 0 012 $\mu g/in^2$ < 0 012 $\mu g/in^2$	< 0 012 $\mu g/in^2$
25 lb/3000 ft^2 uncoated paper sheets treated at 0.75% dry weight FCS	1-H Perfluorohexane	Corn Oil	5 minutes at 700 watts	< 9 0 $\mu g/in^2$ < 9 0 $\mu g/in^2$ < 9 0 $\mu g/in^2$	< 9 0 $\mu g/in^{2*}$
	Perfluorohexane	Corn Oil	5 minutes at 700 watts	< 18 $\mu g/in^2$ < 18 $\mu g/in^2$ < 18 $\mu g/in^2$	< 18 $\mu g/in^{2*}$
	3-perfluoro-n-hexylprop-2-enol	Corn Oil	5 minutes at 700 watts	< 5.0 $\mu g/in^2$ < 5 0 $\mu g/in^2$ < 5 0 $\mu g/in^2$	< 5 0 $\mu g/in^{2*}$
				***As discussed in Section II.E, other data suggests that the thermal degradates will not migrate at a level equivalent to 0.5 $\mu g/in^2$.**	

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d Provide a summary of method validation results Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels Full details, including description of spiking procedure and calculations, must be included as an attachment

The migration studies were validated by spiking the various analytes into aliquots of sample extracts at the respective limits of detection, working up the samples in the same manner as the samples, and then demonstrating that the analytes were adequately detected Additional information on the validation is set forth in **Attachment 5**

Analyte	Corn oil		
	Amount added	**Amount Detected**	**% Recovery**
1,3-DCP	0 012 µg/in^2	0.0126 µg/in^2	105
3-CPD	0 012 µg/in^2	0 019 µg/in^2	151
1H-Perfluorohexane	10 µg/in^2	11 3 µg/in^2	113
Perfluorohexane	18 µg/in^2	17 µg/in^2	94
3-Perfluoro-n-hexylprop-2-enol	4 6 µg/in^2	3 4 µg/in^2	74

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2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II D for discussions on 100% migration calculations, II D 4 for information on FDA's migration database, and II D 5 for migration modeling

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS Fully describe assumptions made in deriving the estimates and show all calculations

Migration of the FCS and its impurities to food has been calculated on a worst-case basis These calculations assume (1) a paper basis weight of 26 mg paper/in^2, (2) treatment level of the paper with 0.75% FCS, and (3) 100% migration of the low molecular weight oligomers (<1000 Daltons) or the residual impurities to 5 g food/in^2

The migration calculations are set forth in **Attachment 3.**

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Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II E and Appendix IV

EDI for the notified use must be calculated by the notifier for both the FCS and any migrants The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS The notifier may wish to consult FDA to obtain this information prior to submitting a notification

1 SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)* If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached The following general equation is used to calculate an EDI

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

See **Attachment 4** for dietary exposure calculations

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II F 2 and the use scenario information described in Section II D 2 b, show the calculations used for determining DC and EDI for the FCS and any migrants

☐ Mark (X) this box if you attach a continuation sheet Enter the attachment name and number in Section VI of this form

000018

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Oligomers	Not Listed	1 5	0 0147	4.4×10^{-5}	0 487
Epichlorohydrin	106-89-8	3 2	0 0032	9.6×10^{-6}	
2,3-DCP	616-23-9	3 2	0 0032	9.6×10^{-6}	
1,3-DCP	96-23-1	2 4	0 0024	7.2×10^{-6}	
3-CPD	96-24-2	2 4	0 0024	7.2×10^{-6}	
TETA	112-24-3	13 2	0 013	3.9×10^{-5}	
Allyl Alcohol	107-18-6	6 7	0 0067	2×10^{-5}	
1H Perfluorohexane	355-37-3	100	0 1	3×10^{-4}	
Perfluorohexane	355-42-0	100	0 1	3×10^{-4}	

(b) (4)

Confidential

Confidential

Confidential

000019

AD

Komolprasert, Vanee

From: Keithline, Jeffrey A. [Keithline@khlaw.com]
Sent: Wednesday, December 12, 2007 5:27 PM
To: Komolprasert, Vanee
Cc: Langhorn, Pamela L.; Keithline, Jeffrey A.; Reichert, William W.
Subject: RE: FCN 783_oil/grease resistant sizing agent (Hurcules Inc.)
Attachments: Response to Questions on FCN No. 783.pdf; Sanitized Response to Questions on FCN No. 783.pdf

Dear Dr. Komalprasert:

Attached, please find our response to the questions that you sent Pam Langhorn on December 3, 2007 regarding Hercules Incorporated's food contact notification for the oil/grease resistant sizing agent for paper and paperboard intended for use in microwave susceptor applications. We trust that you will find that we have been responsive to the questions you raised in your letter. We are also sending copies of both the letter and sanitized version by Federal Express, and you should receive those copies tomorrow.

Should you have any further questions, please do not hesitate to contact Ms. Langhorn or me.

Sincerely,
Jeff Keithline

Jeffrey A. Keithline
Attorney
tel: 202.434.4136 | fax: 202.434.4646 | keithline@khlaw.com
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Writer's Direct Access
Pamela L. Langhorn
(202) 434-4291
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December 12, 2007

Via Electronic and U.S. Mail

Vanee Komolprasert, Ph.D., P.E.
Consumer Safety Officer
Division of Food Contact Notifications (HFS-275)
Office of Food Additive Safety
University Station (CPK2)
4300 River Road
College Park, Maryland 20740-3835

Re: Hercules Incorporated; Response to Agency's Questions on Food Contact Notification No. 783; Our File No. HE03743

Dear Dr. Komolprasert:

The purpose of this letter is to address the issues raised in your December 3, 2007 letter regarding Hercules Incorporated's Food-Contact Notification (FCN) No. 783 for 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine (CAS Reg. No. 464178-94-7). You asked two questions regarding impurities present in the food contact substance (FCS). Below, we have repeated your questions and provide our responses to each.

> *Identifications of Samples. In the TETA analysis, you used samples designated as X34024-41B, X33938-34-4, X33976-97-1 and X33938-26-3. You should identify all samples, with the exception of the sample designated X33938-34-4, specifically indicating the wt-% total solids in each sample.*

The data provided in Attachment 5, pages 5-46 through 5-96, included data on the food contact substance (which was designated in this report as X33938-34-4) as well as other similar products under development by Hercules. The substances identified by product codes X34024-41B, X33976-97-1, and X33938-26-3 were developmental prototypes, which were produced using different manufacturing processes. The level of TETA in these developmental products cannot be correlated to the level of TETA in the final FCS. Data on these developmental samples were included in the FCN simply because testing on these samples was conducted at the same time as the testing on the FCS, and the results were set forth in the same report. Nonetheless, for your reference, the %-solids in the developmental products are as follows:

Product	% solids
X34024-41B	13.2%
X33976-97-1	12.94%
X33938-26-3	14.4%

We note that in the Exygen report (Attachment 5, page 5-46 to 5-96), the summary data table on page 5-65 suggests that the results were reported on a dry weight basis. This was an error. The testing was conducted on liquid samples, including the FCS, X33938-34-4 (14.5% solids), as indicated on page 5-53 of the Exygen report.[1] Nonetheless, this error in the Exygen report does not affect the residual level reported in Form 3480 (*i.e.*, 338 µg/g) which correctly accounted for the solids content of the sample.

(b) (4)

[redacted]

* * *

[1] The chain of custody (page 5-53) indicates that the samples were delivered as liquids.

(b) (4)

[redacted]

Please note that this letter contains confidential business information that should not be released to third parties in accordance with FDA public information regulations. For the Agency's convenience, we have enclosed a sanitized version of this submission from which all claimed confidential information has been deleted; this sanitized version may be used in responding to any requests under the Freedom of Information Act for the notification. If the Agency decides to release any information that we have claimed as confidential, we request that you notify us first in accordance with FDA's Public Information Regulations so that we may exercise our right of appeal.

We trust that you will find this information fully responsive to your requests so that FCN No. 783 will become effective 120 days from the date of its original receipt on November 7, 2007. Should any questions remain, please contact us, preferably by telephone or e-mail, so that we can provide a response at once.

Sincerely yours,

(b) (4)

Pamela L. Langhorn

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: February 8, 2008

From: Division of Food Contact Notifications, Chemistry Review Group 1

Subject: **FCN 783**: Hercules Inc. through Keller and Heckman. Expanded use of 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease-resistant sizing agent in food-contact paper and paperboard intended for use in microwave heat-susceptor packaging. Submissions dated November 6, 2007 (initial submission) and December 12, 2007 (response to deficiencies).

To: Division of Food Contact Notifications, Regulatory Group 2
Attention: V. Komolprasert, Ph.D.

Keller and Heckman (K&H) on behalf of Hercules Inc. (Hercules) submitted this food contact notification (FCN) to expand the use of the food contact substance (FCS) identified as 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine, as an oil/grease-resistant sizing agent employed prior to the sheet-forming operation (internal sizing) and/or at the size press (external sizing) in the manufacture of paper and paperboard.

The FCS, referred to as PPD D-1435 in the FCN, is marketed as an aqueous solution containing 10-15 weight-percent (wt.-%) solids. The FCS will be used at a level not to exceed 0.75% by weight (wt.-%) of the dry paper and paperboard intended for use as a component of microwave heat-susceptor packaging (Condition of Use J as described in Table 2 on our website). The FCN also outlines a modified synthetic method that affects impurity levels in the final product.

Regulatory Status

The FCS is not regulated in 21 CFR 170-199. The FCS was the subject of Hercules's FCN 746[1] (effective October 4, 2007) and 542[2] (effective November 25, 2005). FCN 542 was for use of the FCS, identified as PPD D-1101, as an oil/grease resistant sizing agent employed prior to the sheet-forming operation (internal sizing) in the manufacture of paper and paperboard, at a level not to exceed 0.5 wt.-% of the dry paper and paperboard, intended to contact all foods under Conditions of Use B through H. FCN 746 introduced an improved manufacturing method, expanded the use to include addition at the size press, increased the FCS use level (from 0.5 wt.-% to 0.75 wt.-%) and expanded the conditions of use to include Condition of Use A.

In comparison to the use in FCN 746, the subject FCN includes use in microwave heat-susceptor packaging and serves to introduce a modified manufacturing method.

[1] Chemistry memorandum for FCN 746 dated September 12, 2007 (S. Elyashiv-Barad to V. Komolprasert).
[2] Chemistry memorandum for FCN 542 dated November 15, 2005 (S. Elyashiv-Barad to P. Honigfort).

The FCS is similar to the FCSs described in Hercules's FCNs 314[3] (effective April 23, 2003), (b) (4) 487[4] (effective July 14, 2005) and FCN 518[5] (effective August 23, 2005), with the exception of the (b) (4) component used to manufacture the FCS. *The FCS in FCNs 542, 746 and the subject FCN use* (b) (4) *iodide (a C6 alkyl) while that in FCNs 314,* (b) *487, and 518 used a mixture of* (b) (4) *iodides (C6-C18), as described below.*

1) FCN 314 was submitted for use of 2-propen-1-ol, reaction products with pentafluoroiodoethane-tetrafluoroethylene telomer, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine (identified as PPD D-1085) as an oil/grease resistant sizing agent employed prior to the sheet-forming operation in the manufacture of paper and paperboard. The FCS may be used at a level not to exceed 0.5 wt.-% of dry paper and paperboard in contact with all food under Conditions of Use B through H.

(b) (4)

3) FCN 487 outlined a new synthetic method for the FCS in FCN 314, identified new impurities and new residual levels for previously known impurities, and expanded the use of the FCS to include size press applications (external sizing). The FCS may be used at a level not to exceed 0.5 wt.-% of dry paper and paperboard in contact with all food under Conditions of Use B through H.
4) FCN 518 further modified the manufacturing process described in FCN 487, and expanded the use to include microwave heat-susceptor packaging.

Chemistry information is contained in FDA Form 3480, Attachments 1 (chemical structure), 2 (manufacturing description), 3 (migration calculations), 4 (exposure estimates), 5 (analytical data), and 8 (stability data continuation page), and incorporated by reference from FCNs 542 and 314. New chemistry information is contained in Attachments 2-5 and 8. Additional chemistry information is contained in the December 12, 2007 submission. The notifier provided the suggested language for the proposed use of the FCS in Attachment 6.

Identity

Information on the identity of the FCS is contained in FDA Form 3480, Sections II.A and II.C, Attachments 1 and 5, and FCNs 314 and 542. *This information was previously reviewed and accepted and is summarized below for convenience.*

As indicated in the November 15, 2005 chemistry memorandum for FCN 542, the FCS basically consists of a triethylenetetramine (TETA) backbone onto which are substituted groups derived from allyl alcohol (AA), epichlorohydrin (ECH) and (b) (4) iodide (PFHI).

CAS Name: 2-propen-1-ol, reaction products with 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-6-

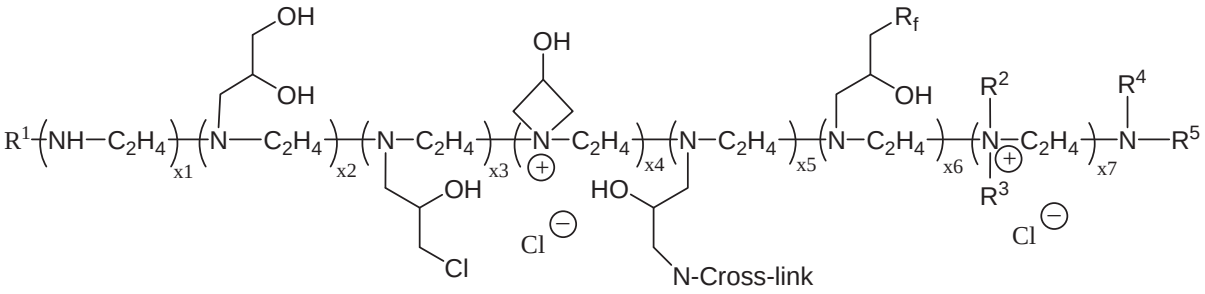
[3] Chemistry memorandum for FCN 314 dated March 17, 2003 (S. Elyashiv-Barad to V. Gilliam).
[4] Chemistry memoranda for FCN 487 dated April 26, 2005 (K. Arvidson to P. Honigfort), June 10, 2005 (K. Arvidson to P. Honigfort) and July 6, 2005 (K. Arvidson to the File).
[5] Chemistry memorandum for FNC 518 dated September 23, 2005 (K. Arvidson to V. Gilliam).

iodohexane, dehydroiodinated, reaction products with epichlorohydrin and triethylenetetramine

CAS Reg. No.: 464178-94-7

Other names: PPD D-1435 (PPD-1101 in FCN 542; PPD D-37614 in FCN 746)

Chemical Structure: (Attachment 1 of the FCN)



R^1-R^5 = H;
$CH_2CH(OH)CH_2OH$;
$CH_2CH(OH)CH_2Cl$;
$CH_2CH(OH)CH_2$(N-Cross-link)
$CH_2CH(OH)CH_2R_f$ where $R_f = (CF_2)_5CF_3$

X_1-X_7 can be in any order (aka random substitution on the TETA backbone)
We presume that the molar ratios of X1:(X2+X3):X4:(X5+X7):X6 = ~11:10:10:30:38, which are identical to those provided in Hercules's previous FCNs.

Molecular weight distribution (MWD)

The weight-average (Mw) and number-average (Mn) molecular weights were reported as 652,612 and 84,570 Daltons, respectively, in Form 3480 (Section II.A) based on the size exclusion chromatography (SEC) data contained in the FCN (see Section IV of Attachment 5). The information in Section IV is identical to that provided in previous FCNs.

As discussed in our November 15, 2005 memorandum on FCN 542, SEC indicated that 2.5 wt.-% of the dry weight of the FCS consisted of low molecular weight oligomers (LMWOs) <1000 Daltons, with about 2.4 wt.-% being <500 Daltons. As described in Attachment 3, and Sections IV and IX of Attachment 5 of the subject FCN, this value was refined by accounting for the presence of residual TETA and the concentration of additional TETA-oligomers formed during microwave-heating. This is described in more detail in the **Migrant Levels in Food** section, below.

Specifications/Properties

Specifications for the FCS (pH, viscosity and wt-% total solids) are provided in Form 3480, Section II.C, and are identical to those reported in FCN 746. The range of total solids reported in the subject

FCN is 10-15 wt-%.

Characterization

As was the case in FCN 746, the notifier referenced Attachment 2 of FCN 542 which contains a proton nuclear magnetic resonance (^{1}H NMR) spectrum that is consistent with the structure of the subject FCS.

We have no questions on the identity of the FCS.

Manufacture

Information concerning the manufacture of the FCS is described in Form 3480, Section II.B, and Attachments 2 and 5. Raw materials used in the manufacture of the FCS are tabulated in Section II.B and summarized in Table 1, below. The materials are identical to those employed in FCNs 746 and 542.

Table 1: Raw materials used in the manufacture of the FCS

Chemical	CAS No.	Function
(b) (4) iodide (PFHI, aka C6 telomer iodide)	355-43-1	Starting material
Allyl alcohol (AA)	107-18-6	Starting material
(b) (4)		Reagent
Triethylenetetramine (TETA)	112-24-3	Starting material
Epichlorohydrin (ECH)	106-89-8	Starting material
(b) (4)		Process aid
		Process aid
		Catalyst
		Solvent

The manufacturing process is described in Attachment 2. *The reaction chemistry of the FCS is similar to that in FCNs 542 and 746 with the following exceptions*:

1) PFHI is *optionally* distilled to reduce the level of (b) (4) This step is not present in FCN 542 and is present in FCN 746, *not as an optional step, rather as an obligatory step*.
2) Prior to ECH addition, the reaction mixture is steam stripped to reduce the level of 3-(l(b) (4) n the FCS. This step is not present in FCN 542 and is present in FCN 746. We note that FCN 746 also included a step whereby the final product is membrane treated to remove non-fluorinated low molecular weight impurities.

The manufacturing process for the FCS is a multi-step process. All mole equivalents (mol equiv) and wt.-% (in the case of water) are expressed relative to the moles or weight of PFHI.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Information on impurities in the FCS, including typical residual levels, as taken from Form 3480, Section II.B.3 and Attachment 5, is shown in Table 2 below. The reported impurity levels are based on the analysis of an FCS containing 14.5 wt.-% total solids (b) (4)

We note that a comparison of the levels reported for the subject FCN and previous FCNs (746 and 542) indicates no specific pattern regarding impurity levels in the FCS, as some impurity levels in the subject FCN are lower while others are higher than those reported in the previous FCNs.

Table 2: Typical levels of impurities in the FCS (compared to that in FCNs 746 and 542)

Impurity	CAS Reg. No.	FCN 783: Typical residual (dry basis, mg/kg)	FCN 746: Typical residual (dry basis, mg/kg)	FCN 542: Typical residual (dry basis, mg/kg)
PFHI	355-43-1	<172	<169	308
3-(b) (4) 2-iodopropan-1-ol (C6 iodohydrin)	38550-44-6	<172	<169	<94
(b) (4) (b) (4)				
AA	107-18-6	<172	<169	3900
ECH	106-89-8	<83	1.4	<30
1,3-Dichloro-1-propanol (1,3-DCP)[a]	96-23-1	7170	1180	991
(b) (4)				
TETA	112-24-3	417.2[c]	154	Unknown
(b)(b) (4)				
Hydrolysis product of ECH.				
(b) (4) (b) (4)				

Section II of Attachment 5 contains adequate supporting data, including the analytical methods and

raw data, for PFHI, [redacted] AA, chloropropanols (ECH; [redacted] The average level of TETA was mistakenly reported as ~50 µg/g FCS on a "wet basis" rather than 57.4 µg/g FCS on a "wet basis". The methods contained in Section II of Attachment 5 were reviewed and accepted in our review of previous FCNs.

In response to your December 3, 2007 deficiency letter, the December 12, 2007 submission provided information on the solids content of the samples used in the TETA analysis (X34024-41B, 13.2% solids; X33976-97-1, 12.94% solids; and X33938-26-3, 14.4% solids). The December 12, 2007 submission also confirmed that the impurity levels in Form 3480 were reported on a "dry basis" of FCS, while those in Attachment 5 were reported on a "wet basis".

We have no questions on the manufacture of and impurities in the FCS.

Intended Use and Technical Effect

Information concerning the intended use and technical effect of the FCS is discussed in Form 3480, Section II.D, and FCN 314.

The FCS is intended for use as an oil/grease-resistant sizing agent at levels up to 0.75% in paper and paperboard intended for use in microwave heat-susceptor packaging. The FCS is intended to be added to the paper prior to the sheet-forming operation or at the size press. The notifier provided data in Attachment 6 of FCN 314 supporting the grease-resistant properties of the FCS. This data was previously used to support the proposed use in FCN 518.

According to the Hercules website,[7] the imPress™ ST surface size technology line of products are cellulose reactive, surface sizing agents designed to impart high levels of sizing for a variety of applications. Cellulose reactive sizes, such as alkylketene dimer (AKD) and alkenyl succinic anhydride (ASA), have reactive sites that form covalent bonds with hydroxyl groups on cellulose. Similarly, the FCS reacts with hydroxyl groups present on the size press starch and the base sheet fiber. This reaction delivers a high level of sizing that is unmatched by traditional surface sizes. ImPress products are reported to be low foaming, are compatible with most size press additives, and enable the paper manufacturer to change the balance between wet-end (internal) and surface (external) size addition.

We have no questions about the intended use and technical effect of the FCS.

Stability

[6] This sample was manufactured with non-distilled PFHI.
[7] http://ppd herc.com/innovations/impress™_sizing_and_printability_technology_.asp

Information on the stability of the FCS is provided in Form 3480, Section II.E, and Attachments 5 and 8.

The notifier indicated that the FCS is thermally unstable under the intended conditions of use, as was the case in FCN 518. The notifier provided studies (dated November 29, 2006 and March 14, 2007) on the characterization and migration of thermal degradation products in Sections VI-VII of Attachment 5.

Thermogravimetric analyses (TGA) of the FCS in air was conducted to determine the degree of weight loss when exposed to a heating profile similar to microwave conditions, *i.e.*, reaching 240°C in approximately 3 minutes in air (see Section VI of Attachment 5). The reported weight loss values at 220, 225, 233 and 240°C were 10.4, 12.3, 16.6, and 20.9%, respectively, and were similar to those reported for the related FCS in FCN 518. We note that while the sample used in this study was specifically identified as Impress FP 200, the FCS in FCN 746, we believe that this study is applicable to the subject FCN.

As indicated in the September 23, 2005 chemistry memorandum for FCN 518, given that the experiments were performed on neat samples of the FCS, we would expect the TGA results to represent a worst-case scenario for the decomposition of the FCS under conditions of microwave heating. Therefore, we believe that under actual use conditions, a majority of the FCS would be exposed to large volumes of steam (100°C) rather than contacting the susceptor-heated oil. Examination of the TGA curve (Figure 1 in Section VI of Attachment 5) shows less than 5% weight loss of the polymer at 100°C. Therefore, as in FCN 518, we would expect ≤5% breakdown of the FCS during use of a popcorn bag.

The notifier also qualitatively identified volatile thermal degradation products of the FCS upon heating up to 240°C (see Section VII of Attachment 5). (b) (4) (b) (4) (b) (4) We note that several thermal degradation products were also identified in FCN 518.

We have no questions regarding the stability of the FCS.

Migrant Levels in Food

Studies to estimate migrant levels in food under microwave susceptor use conditions were briefly described in Form 3480, Section II.F, with the full report contained in Sections III (migration of 1,3-DCP and 3-CPD), V (migration of (b) (4) and VIII (migration of thermal degradates) of Attachment 5. Attachment 3 and Sections IV and IX of Attachment 5 describe the approach used to determine the fraction of LMWOs in the FCS, later used to estimate levels in food based on 100% migration. The migration protocol used in Sections III and VIII of Attachment 5 is identical to that submitted in support of FCN 518 and previously reviewed and accepted by FDA, and the LMWO studies are identical to those reported in previous FCNs. All studies are summarized below.

(b) (4)

(b) (4)

[redacted]

Migration of (b) (4) [redacted]

Migration studies were carried out on a paper sample (1 x 1 inch squares) treated with the FCS[9] (0.75%) under microwave heat susceptor conditions. Studies with an untreated sample of paper were also carried out as controls.

Paper samples (1 x 1 inch squares) were prepared by gluing a microwave susceptor (1 x 1 inch square) to one side of the square. The sample was placed into a 50-ml propylene centrifuge tube with water (0.75 g intended to mimic the water content of popcorn) and heated in a 700 watt microwave on high for 5 minutes. A glass beaker containing water (500 mL) was used as a load. After heating, the samples were cooled and 9 ml of methanol were added. The tubes were then capped and shaken for one hour. Aliquots (work-up not clearly described) were analyzed (in

[8] 31.25 mL/20 mL = 1.55

[9] The notifier indicated that the telomer iodide raw material used to manufacture the FCS was distilled to remove (b) and the Rf-TETA intermediate was steam-treated to remove the unsaturated telomer acohol.

triplicate) for (b) (4) using liquid chromatography (LC)/mass spectroscopy (MS)/MS using a reported m/z range of 313 to 329 (decarboxylation of $[M-H]^-$).

A calibration curve for (b) (4) was generated using a series of standards ranging in concentration from 1.1-109 ng (b) (4) mL. (b) (4) was not detected in the extracts at 11 ng/mL. Using the aliquot volume (25 mL), dilution factor (2),[10] and surface area (1 in^2), a standard concentration of 0.011 µg/mL corresponds to 0.55 $µg/in^2$.

One of the test samples was spiked with 0.28 µg and 0.55 µg (b) (4) followed by work-up and analysis as described above. (b) (4) was detected at the lowest spiking level, while the recovery at the higher level averaged 95%. The method was adequately validated.

Migration of FCS Thermal Degradates (Section VIII of Attachment 5)

Migration studies, identical to those described for (b) (4) and (b) (4) were carried out for the degradation products 1H-(b) (4) and (b) (4) (el d in the TGA-MS analysis of the FCS), and (b) (4) (in order to increase the range of polarity of other potential degradation products that may not have been detected in the TGA-MS analysis).

Paper samples were folded to produce a 2.5 by 2.5 inch tray (total area 6.25 in^2) and a microwave susceptor glued to the bottom of the tray as above. Oil (29 mL) was added and the paper trays were heated in a 700 watt microwave on high for 5 minutes with a water load. After cooling, aliquots (2 g) were placed in a headspace vial, extracted by solid phase microextraction (SPE) and analyzed by GC with an FID detector. Methods for all three analytes are contained in Section VIII.

Calibration curves for 1H-(b) (4) and (b) (4) were generated using a series of standards ranging in concentration from 1.0-7.7 µg 1H-(b) (4) g, 3.4-26.9 µg (b) (4) g, and 1.07-21.48 µg C6 alcohol/g. The calibration standards were prepared by sequential dilution of stock solutions of the analytes. Given that the oil mass was 29 g and the paper surface area was 6.25 in^2, a standard concentration of 3.4 µg/g corresponds to about 16 $µg/in^2$.

The degradates were not detected in the migration solutions (no visible peak areas). The average migration was reported as <9, <18, and <5 $µg/in^2$ for 1H-(b) (4) and C6 alcohol, respectively. In other words, the three analytes were not detected at the levels of the lowest calibration standards. The method was adequately validated.

In footnote 1 in Attachment 4, the notifier indicated that rather than relying on the non-detect levels of the degradates that resulted from poor method sensitivity, the notifier referred to migration data generated in FCN 518. This data demonstrated that an analogous (b) (4) thermal degradate, 1H-(b) (4) did not migrate to food simulants under microwave susceptor conditions, at a detection limit equivalent to 0.5 $µg/in^2$. Thus, the notifier concluded that the worst-case migration of the thermal degradates would be <0.5 $µg/in^2$. We concur with the notifier's claim.

[10] The final volume and dilution factor were taken from the table in Attachment V. However, their origin is not clear from the text in the report.

Low-Molecular-Weight Oligomers (LMWOs) Containing TETA, <1000 Daltons (Attachment 3 and Sections IV and IX of Attachment 5)

The notifier did not analyze the test extracts described above for LMWOs. Rather, migration of LMWOs was based on the wt-% present in the FCS and the assumption of 100% migration to food (see below). *This approach was used in Hercules's previous FCNs.*

Size exclusion chromatography (SEC) showed that 2.5% of the dry weight of the FCS consisted of LMWOs with a MW<1000 Daltons. The LMWO fraction was further analyzed by proton (^{1}H) NMR to determine the amount of all TETA-related components contained in the fraction. The notifier noted that this technique was previously described and validated in FCN 314. The level of LMWOs containing TETA was found to be 14,800 μg/g LMWO (ppm based on the total solids weight). Therefore, the LMWO fraction composed solely of TETA-containing oligomers (MW <1000 Daltons) was 374 μg/g FCS (2.5% x 14,800 μg/g). A description of the analytical methods and corresponding spectra were provided in Section IV of Attachment 5.

In Section IX of Attachment 5, the notifier determined the concentration of TETA-oligomers *formed during microwave-heating*. Condensate material collected during thermal degradation of the FCS was quantified by proton NMR against an internal standard. Analysis of the spectra showed signals associated with TETA at 2.8-3.5 ppm. The notifier then quantified the TETA-oligomers using the integration from the standard (hexamethyldisiloxane) and the TETA-oligomers, the respective formula weights of the standard and TETA-oligomers,[11] the amount of sample used and the amount of standard added to the sample, and the wt.-% TETA containing materials in the FCS. The notifier determined that ~0.23-0.43% (average of 0.33%) *new* TETA-oligomers were produced during heating of the FCS under conditions simulating microwave oven conditions. As described in Attachment 8, this is equivalent to ~340 ppm since approximately 10% of the FCS was lost on heating to 220ºC. *This approach was used in FCN 518.*

In Attachment 3, the notifier corrected the LMWO containing TETA (<1000 Daltons) for the residual level of TETA in the FCS (338 μg/g) and the concentration of additional TETA-oligomers formed during microwave-heating (340 μg/g). The corrected LMWO containing TETA (<1000 Daltons) was reported by the notifier as 378 μg/g based on the "dry weight" of the polymer (or 376 μg/g – 338 μg/g + 340 μg/g). While we agree with the notifier's approach, we recalculated the corrected LMWO containing TETA (298.8 μg/g) using the residual TETA level we reported in Table 2 (417 μg/g).

As stated in previous chemistry memoranda for Hercules FCNs, we believe that the remaining fraction of LMWO would contain fluorinated species. Exposure to the fluorinated containing-LMWOs would be accounted for in the exposure estimates to other fluorinated impurities, such as C6 iodohydrin, C6 epoxide and C6 alcohol determined below.

[11] The notifier used 1000 Daltons as an estimate for the molecular weight of the oligomers of concern, we agree with this assumption.

We have no questions about the studies used to determine migrant levels in food.

Consumer Exposure

Information on exposure estimates for the FCS and other migrants is summarized in Form 3480, Section II.G, and supporting information is contained in Attachments 3 and 4. Exposure estimates were estimated based on actual migration results or the assumption of 100% migration to food, as presented below, and summarized in Table 3. This approach was used in Hercules's previous FCNs. On the whole we concur with the notifier's approach to estimating exposure.

(b) (4) and (b) (4)

The notifier estimated exposure to these substances based on the non-detect migration values obtained from the corn oil migration experiments (<0.012 μg/in^2 for both 1,3-DCP and 3-CDP, and <0.5 μg/in^2 for both 1H-(b) (4) and (b) (4) and the consumption factor (CF) for microwave susceptor packaging (0.001). The concentrations of the migrants (in μg/in^2) were converted to concentration in food by multiplying by FDA's assumption that 5 g of food contacts 1 square inch of microwave susceptor packaging.

Exposure estimates for 1,3-DCP, 3-CPD, 1H-(b) (4) and (b) (4) are summarized in Table 3.

TETA-containing LMWOs, TETA, PFHI, (b) (4), AA, ECH, (b) (4), (b) (4) and (b) (4)

Exposure estimates were based on the assumption of 100% migration to food and the following information:

1) a basis weight of 26 mg/in^2 for popcorn bags,
2) the maximum use level of the FCS (0.75%, or 0.0075 mg FCS/mg paper),
3) the residue levels for impurities shown in Table 2, above, and for TETA-containing LMWOs, also above,
4) FDA's assumption that 5 g of food contacts 1 square inch of microwave susceptor packaging, and
5) the CF for microwave susceptor packaging (0.001).

Exposure estimates for TETA-containing LMWOs, TETA, PFHI, (b) (4) AA, ECH, (b) (4) (b) (4) and (b) (4) are tabulated in Table 3.

C6 alcohol

The notifier estimated exposure based on the assumption of 100% migration to food. We note however, that the notifier also carried out migration studies on thermal degradates which resulted in a migration value of <5μg/in^2 for C6 alcohol. The DC based on actual migration results (1 ppb) is higher than the DC estimated using the assumption of 100% migration (13 pptr).

(b) (4)

We note that AIBN is cleared in 21 CFR 176.170 for use in the manufacture of paper and paperboard.

Summary of Exposure Estimates

Exposure estimates are summarized in Table 3 below. For comparison, we also included in Table 3 estimates from FCNs 746 and 542. With the exception of LMWO containing TETA (<1000 Daltons) and TETA, the exposure estimates summarized in Table 3 are not significantly different that those reported by the notifier.

Table 3: Summary of exposure estimates

Substance	FCN 783: DC (ng/kg or pptr)	FCN 746: DC (ng/kg or pptr)	FCN 542: DC (ng/kg or pptr)
LMWOs containing TETA (<1000 Daltons)	11.7	450	470
PFHI	6.7	<3.9[a]	4.7[c]
(b) (4)	6.7	<3.8[a]	1.4[c]
	6.7	<3.8[a]	1.4[c]
	13	<0.5[b]	<500[b]
AA	6.7	<0.5[b]	<500[b]
ECH	3.2	<0.03[a]	0.46[c]
(b) (4)	2.4	<13[b]	<10[b]
	3.2	0.03[a]	0.06[c]
	2.4	70[b]	<18[b]
TETA	16.3	<15[b]	<50[b]
(b) (4)	1.3	1.8[a]	1.4[c]
(b) (4)	0.3[e]	<0.02	0.1[d]
(b) (4)) (4)	0.1	---	---
	0.1	---	---

[a] Determined as described in the text.
[b] Based on migration studies.
[c] Based on the "wet-end" model.
[d] Not addressed in FCN 542, estimated at 0.1 ng/kg as discussed in the text.
[e] As indicated in the **Manufacture** section above, we used the maximum level of (b) (4) to estimate exposure.

Comments on Cumulative Exposure

In our September 12, 2007 memorandum for FCN 746, we noted that the uses of the subject FCS (manufactured by Hercules from PFHI and the subject of FCNs 542 and 746, would "substitute" for

the uses and FCS manufactured by Hercules from a mixture of (b) (4) iodides and the subject of FCNs 314 and 487. The conclusion also holds true for the subject FCS and use in FCN 783 when compared to the FCS and use in FCN 518. Moreover, the subject FCS and uses would also "substitute" for similar greaseproofing agents and uses that are permitted for use in contact with food.

In our September 12, 2007 memorandum, we concluded that a DC of 0.45 ppb for LMWOs containing TETA units (<1000 Daltons) would represent both FCNs 542 and 746. The use in FCN 783 represents a new use for the FCS and would result in a negligible increase in the cumulative exposure for the LMWOs containing TETA (<1000 Daltons). Thus, the cumulative dietary concentration (CDC) for LMWO containing TETA (<1000 Daltons) for FCNs 542, 746 and 783 would remain at 0.45 ppb, corresponding to a cumulative estimated daily intake (CEDI) of 1.4 µg/p/d.

In our September 12, 2007 memorandum for FCN 746, we also concluded that the *highest* DC value for each individual impurity in the FCS (as shown in Table 5 in that memorandum) would represent the cumulative exposure for each impurity for both FCNs 542 and 746. For the subject FCN, the new CDC for each impurity in the FCS would be the sum of the current CDC and the DC from the subject FCN. Cumulative impurity exposure estimates are summarized in Table 4, below.

Table 4: Cumulative impurity exposure estimates

Substance	Current CDC[a] (ng/kg or pptr)	New CDC[b] (ng/kg or pptr)
PFHI	4.7	11.4
(b) (4)	<3.8	10.5
	<3.8	10.5
	<500	<513
AA	<500	<507
ECH	0.46	3.7
(b) (4)	<13	15.4
	0.06	3.3
	70	72.4
TETA	<50	66.3
(b) (4)	1.8	3.1
(b) (4)	0.1	0.4
(b) (4)	---	0.1
(b) (4)	---	0.1

[a] The current CDC for each impurity represents the *highest* DC value for each impurity for FCNs 542 and 746.
[b] The new CDCs were calculated by summing the the current impurity CDC and the impurity DC from the subject FCN (provided in Table 3, above).

Notification Language

The acknowledgment letter dated December 14, 2007 is appropriate as written.

Conclusion

We have no questions on this FCN.

Sharon Elyashiv-Barad

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Reading File); HFS-705 (Diachenko)
HFS-275:SElyashiv-Barad:301-436-1169:seb:2-8-08 (FCN783_C_memo)
RDInit: ABBailey, 2/8/08
Final: seb, 2/8/08

CH

Attachments

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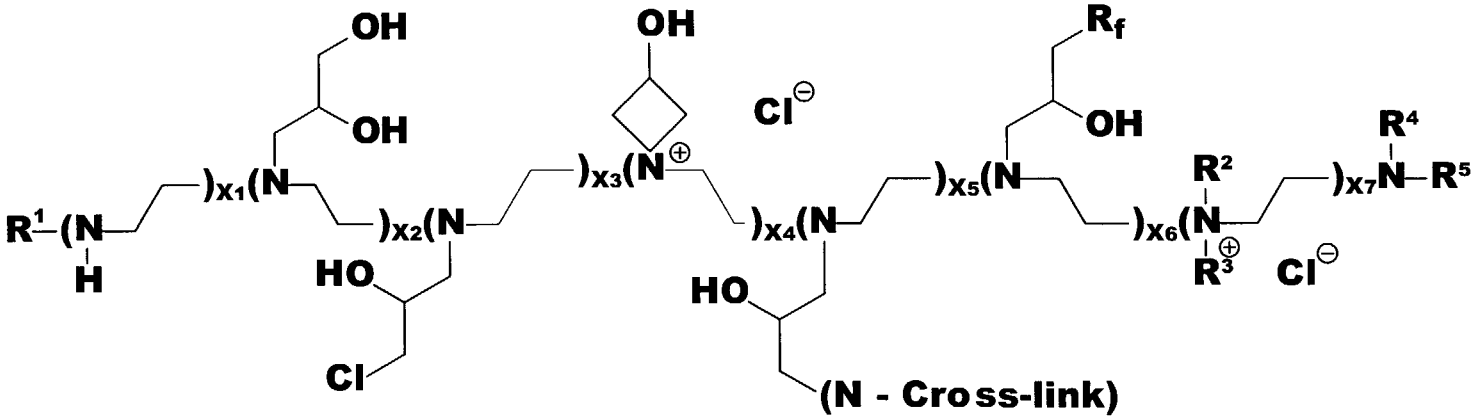
1

D-1101 Oil Size Polymer



D-1101 Oil Size Polymer

R^1- R^5 = H, $CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2Cl$,
$CH_2CH(OH)CH_2$(N-Cross-link), $CH_2CH(OH)CH_2R_f$

$R_f = F(CF_2)_6$

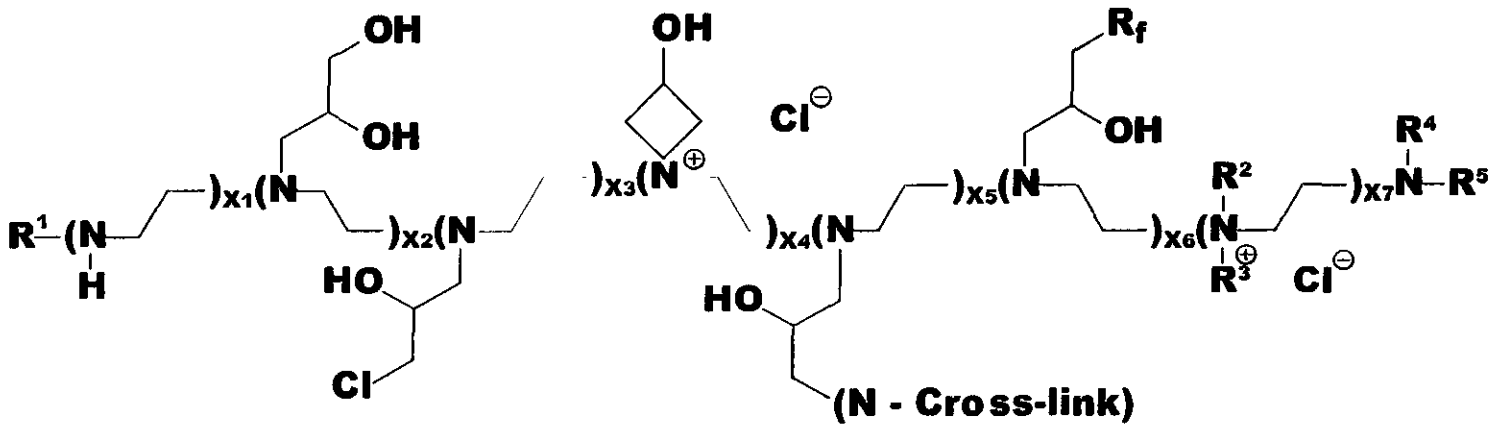
X_1 - X_7 Can be in any order

CH

1

000023

D-37614 Oil Size Polymer



R^1- R^5 = H, $CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2Cl$,
$CH_2CH(OH)CH_2$(N-Cross-link), $CH_2CH(OH)CH_2R_f$

$R_f = F(CF_2)_6$

X_1 - X_7 Can be in any order

000024

C. Chemical Identity Of Food Contact Substance

Fluorinated polyurethane anionic resin prepared by reacting perfluoropolyether diol (CASRN 88645-29-8), isophorone diisocyanate (CASRN 4098-71-9), 2,2-dimethylolpropionic acid (CASRN 4767-03-7) and triethylamine (CASRN 121-44-8).

Chemical Abstracts Name:

Propanoic acid, 3-hydroxy-2-(hydroxymethyl)-2-methyl-, polymers with 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane and reduced Me esters of reduced polymd. oxidized tetrafluoroethylene, compds. with triethylamine.

CAS Registry Number: 328389-91-9.

The weight average molecular weight of the polymer is about 21,000 daltons; the number average weight is about 14,000 daltons. Gel permeation chromatography (GPC) shows that the fraction of the polymer having molecular weights lower than 1000 daltons is not more than 0.1% of the polymer. Representative GPC chromatogram's from two batches of PT 5060 polymer are provided in Appendix 1. An infrared spectrum is provided as Appendix 2. A representative structure of the polymer is provided as Appendix 3.

Specifications for Fluorolink PT 5060 are provided in the Safety Data Sheet, Appendix 4.

Preparation of Fluorinated Polyurethane Anionic Resin

The resin is prepared by reacting a perfluoropolyether diol (CAS Reg. No. 88645-29-8) with isophorone diisocyanate to form a prepolymer. The prepolymer is then

reacted with 2,2-dimethylolpropionic acid to form the polymer of desired chain length. Triethylamine is added to partially neutralize the polymer and form the water dispersion.

The complete manufacturing process is provided as a **Confidential Appendix** (Appendix 5) to this Notification. The perfluoropolyether diol is manufactured by AUSIMONT as an intermediate. The Chemical Abstracts Name for this polymer is "ethane, tetrafluoro-, oxidized, polymd., Me esters reduced" The weight average molecular weight of perfluoroether diol is about 2000 daltons; the number average molecular weight is 1500 daltons. Although it is a starting material, not the finished product, a description of the manufacturing process for this polymer is also provided in the Confidential Appendix.

MSDS data sheets are provided for the starting materials in Appendix 6.

Potential Impurities in Fluorinated Polyurethane Anionic Resin

Potential impurities and their source are shown in the following table:

Impurity	CASRN	Source
Isophorone Diisocyanate	4098-71-9	Monomer
Dibutyltin Dilaurate	77-58-7	Catalyst
Perfluoroether Diol	88645-29-8	"Monomer"
Methyl Ethyl Ketone	78-93-3	Solvent
2,2-Dimethylolpropionic Acid	4767-03-7	Monomer
Triethylamine	121-44-8	Neutralizing Agent
Isopropanol	67-63-0	Solvent

Based on analytical methodology used to monitor the manufacturing process, concentration of solvents (isopropanol and methyl ethyl ketone) will be less than 4 % by weight of dry polymer, although actual concentrations are undoubtedly lower. When PT 5060 polymer is added at the wet end, the concentration of solvents in paper will be negligible. Even if applied at the size press, the solvents and triethylamine should be

removed when the paper is steam dried. (Respective boiling points for isopropanol, methyl ethyl ketone, and triethylamine are 82°C, 80°C, and 89°C.)

Both isopropanol and methyl ethyl ketone have direct clearances in the food additive regulations. Isopropanol is cleared as a direct or secondary direct food additive under 21 C.F.R. § 172.515 as a synthetic flavoring substance; under 21 C.F.R. § 172.560 in the manufacture of modified hop extract; and under 21 C.F.R. § 173.240 as a residue in spice oleoresins at a maximum 50 ppm, in lemon oil at a maximum 6 ppm, and in hop extracts at a maximum of 2%. Methyl ethyl ketone is also cleared under 21 C.F.R. § 172.515 and under 21 C.F.R. § 172.859 at a maximum level of 10 ppm in sucrose fatty acid esters.

Triethylamine has no direct food additive clearances, but is cleared as a reactant employed in the production of polyurethane resins under 21 C.F.R. § 175.105 and as an optional adjuvant in the production of polycarbonates under 21 C.F.R. § 177.1580. Isophorone diisocyanate is cleared under 21 C.F.R. § 177.1680 (Polyurethane resins, as 3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate) and as components of adhesives intended for use in high temperature laminates under 21 C.F.R. § 177.1390. 2,2-Dimethylolpropionic acid is cleared in 21 C.F.R. § 175.105 as a monomer in polyurethane resins and as a pigment dispersant in 21 C.F.R. § 178.3725. Dibutyltin dilaurate is cleared for use in the preparation of polyurethane resins under 21 C.F.R. § 175.105 and is cleared as an optional adjuvant under 21 C.F.R. § 177.1680 (Polyurethane resins).

SOLVAY SPECIALTY FCN 187

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

U.S. Food and Drug Administration, Washington, D.C. 20204

Memorandum

AD

Date January 17, 2002

From Division of Food Contact Substance Notification Review (DFCSN)

Subject Review of fluorinated polyurethane anionic resin (25-30% aqueous dispersion, Fluorolink PT 5060) prepared by reacting perfluoropolyether diol, isophorone diisocyanate, and 2,2-dimethylolpropionic acid in the manufacturing of paper and paperboard.

To FCN 187 File

Through Carolyn Young, Ph.D. Carolyn Young
Acting Supervisor, Toxicology Group 2, DFCSN

FOOD CONTACT NOTIFICATION No. 187

Ausimont SpA
Viale Lombardia 20
20021 Bollate (Milano), Italy
02-3835-6227 (T) 02-3835-6302 (F)
Via Keller and Heckman LLP

A toxicology study submitted in support of FCN 187 was reviewed by Pitner Anderson, MEM, and Kara Altshuler, Ph.D., at ICF [Contract No. 223-00-2450, Work Assignment No. 2001-38 (ICF 038). The study, "Fluorolink PT 5060 Bacterial Mutation Assay (*S. typhimurium* and *E. Coli*)", is contained in FCN 187 (pages 128 - 174) and was conducted by Research Toxicology Centre (RTC) S.p.A., Genetic Toxicology Department (Pomezia, Italy) for AUSIMONT S.p.A.

The TDERs are acceptable as final.

Michelle L. Twaroski, Ph.D.
Cc:DFCSN (Young, Varner, Johnson, Twaroski)

000345

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
U.S. Food and Drug Administration, Washington, D.C. 20204

AD

Memorandum

Date March 15, 2002

From Division of Food Contact Substance Notification Review (DFCSN)

Subject FCN 187, use fluorinated polyurethane anionic resin, prepared by reacting perfluoropolyether diol, isophorone diisocyanate, and 2,2-dimethylolpropionic acid in the manufacturing of paper and paperboard.

To Regulatory Group 2-DFCSN,
Attn.: Parvin M. Yasaei, Ph.D., CSO, CFSAN/OFAS/DFCSN

Through Carolyn Young, Ph.D.
Acting Supervisor, DFCSN, Toxicology Group 2

FOOD CONTACT NOTIFICATION No. 187

Ausimont SpA
Viale Lombardia 20
20021 Bollate (Milano), Italy
02-3835-6227 (T) 02-3835-6302 (F)

Submitted via Ralph A. Simmons
Keller and Heckman LLP
1001 G Street, N.W.
Suite 500 West
Washington, D.C. 20001
202.434.4100 (T) 202.434.4646 (F)

RELATED PETITIONS/NOTIFICATIONS

There are no pending food additive petitions or effective notifications and no regulated uses for the food contact substance (FCS).

PROPOSED USE

Keller and Heckman, on behalf of Ausimont SpA, are notifying to use fluorinated polyurethane anionic resin, prepared by reacting perfluoropolyether diol, isophorone diisocyanate, and 2,2-dimethylolpropionic acid in the manufacturing of paper and paperboard. The final product of use will be a 25-30% aqueous dispersion, Fluorolink PT 5060 (PT 5060 polymer). Ausimont SpA has indicated that the dried resin will be used at levels of less than or equal to 1.5% by weight of the finished dry paper or paperboard, with no food type restrictions and under use conditions B (boiling water sterilized) through H (frozen), as described in Tables 1 and 2 of 21CFR§ 176.170(c), respectively. Using PT5060 polymer at this level imparts increased oil and water repellence to the paper and paperboard.

FOOD CONTACT SUBSTANCE

1. Name: Propanoic acid, 3-hydroxy-2-(hydroxymethyl)-2-methyl-, polymers with 5-isocyanato-1 -(isocyanatomethyl)- 1,3,3-trimethylcyclohexane and reduced Me esters of reduced polymerized oxidized tetrafluoroethylene, compounds with triethylamine.
2. Other Names: Fluorolink PT 5060[1], PT 5060 polymer[2]
3. CAS No.: 328389-91-9
4. Weight average MW: 10,000 – 14,000 daltons[3]
5. Number average MW: 5,000 – 8,000 daltons
6. Percent of polymer < 1000 daltons: 0.16 wt-%
7. Representative structure: A representative structure of polymer presented in Appendix III of the submission.
8. Manufacturing process: The polymer is manufactured by reacting perfluoropolyether diol[4], isophorone diisocyanate, and

Chemicals used in the synthesis of the PT 5060 polymer are listed below:

CHEMICAL	CAS NO.
Isophorone diisocyanate (IPDI)	4098-71-9
Methyl ethyl ketone (MEK)	78-93-3
Perfluoropolyether diol (PFPED)	88645-29-8
Dibutyltin dilaurate (DBTDL)	77-58-7
2,2-dimehylol-propionic acid (DMPA)	4767-03-7
Triethylamine (TEA)	121-44-8
Isopropyl alcohol (IPA)	67-63-0

The table below lists the chemicals involved in the synthesis of perfluoroether diol (CAS No. 88645-29-8):

CHEMICAL	CAS NO.

9. Impurities: The notifier identified several reagents as possible impurities in the FCS. The potential impurities and their respective roles in the manufacture of the FCS are listed in the table below (table obtained from Costantino, Arvidson/Yasaei, 3/12/2002, RE FCN187):

REAGENT	SOURCE
IPDI	Monomer
DBTDL	Catalyst
PFPED	"monomer"
MEK	Solvent
DMPA	Monomer
TEA	Neutralizing agent
IPA	Solvent

[1] Fluorolink PT 5060 is the trade name for a 25 – 30% aqueous dispersion of the anionic resin.
[2] TP 5060 is the trade name for the dried anionic polymer.
[3] Molecular weight data were calculated from gel permeation chromatography (GPC) data contained in the notification by Dr. Costantino (Costantino, Arvidson/Yasaei, 03/12/2002, RE FCN 187).
[4] Manufactured by Ausimont as an intermediate. The CAS name is "ethane, tetrafluoro-, oxidized, polymd., ME esters reduced. The weight average MW of perfluoroether diol is 2000 daltons and the number average MW is 1500 daltons.

10. Technical effect: Data in the notification conducted on paper with 0 to 1.5% by weight of the FCS demonstrates that the FCS imparts oil repellence (Kit test) and inhibits water absorption ($Cobb_{60}$ test).

CURRENT USE AND CUMULATIVE ESTIMAED DAILY INTAKE (EDI)

FCS: There are no current uses for the FCS. Accordingly, the EDI from FCN 187 will be the CEDI. The notifier presents three methods for determining the migration of the low molecular fraction of the resin (< 1000 daltons); therefore, resulting in three EDIs. Accordingly, the EDI for the FCS was estimated using solubility, gel permeation chromatography (GPC), and computer modeling data. Chemistry chose to calculate the EDI using GPC and solubility data and assuming 100% migration (Costantino, Arvidson/Yasaei, 3/12/2002, RE FCN 187). Accordingly, the EDI for low molecular weight oligomers is 72 µg/p/d or 22 µg/p/d calculated using GPC or solubility data, respectively. According to Chemistry, solubility data result in a more realistic exposure estimate; therefore, the EDI of the low molecular weight oligomers of the FCS is 22 µg/p/d (dietary concentration of 7.2 ppb).

Impurities: Impurities are listed in the table below with their EDIs, dietary concentrations (DC), regulatory status and current CEDI (if known). The exposures to MEK, IPA, and TEA are expected to be essentially zero (Costantino, Arvidson/Yasaei).

CHEMICAL	EDI (µg/p/d)	DC (ppb)	CFR DOCUMENTS	CEDI
PFPED[5]	22	< 7.2	no related documents	
IDPI[6]	1.1	0.38	§177.1680 (polyurethane resins in contact with dry food) §177.1390 (high temperature laminates)	
DMPA	1.8	0.6	§176.170 (prior sanction for polyesters in paper) §175.105 (adhesives) §178.3725 (pigment dispersants)	110 µg/p/d[7]
DBTDL	0.20	0.067	§175.105 (adhesives) §177.1680(b) (Polyurethane resins, optional adjuvant)	

CURRENT ACCEPTABLE DAILY INTAKE (ADI) AND BASIS

No ADI is available for the FCS.

TOXICOLOGY

- FCS: For the proposed use of Fluorolink PT 5060, Ausimont SpA submitted one mutagenicity assay as well as a statement indicating that the mutagenic and carcinogenic potential of the monomers should be considered adequate predictors of the carcinogenic risk to the low MW, toxicologically relevant portion of the polymer. The conclusion of the submitted study is provided below.
  - Mutagenicity assay of Fluorolink PT 5060:
    - Fluorolink PT 5060 Bacterial Mutation Assay (*S. typhimurium* and *E. coli*).
      - The study report and data are contained in FCN 187 on pages numbered 127 – 174.
      - Research Toxicology Center (RTC) S.p.A., Genetic Toxicology Department (Pomezia, Italy) conducted the study in 2001.

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[5] The data described for the low molecular weight oligomers of the FCS include those for the polymeric starting material, PFPED, which has an average molecular weight of ~2000 daltons. Applying the exposure of the low molecular weight oligomers of the FCS to that of PFPED is a "very conservative estimate" (Costantino, Arvidson/Yasaei, 03/12/2002, RE FCN 187).

[6] According to Chemistry, IDPI readily hydrolyzes to isophorone diamine (IDPA) in the presence of water; therefore, the migration of IDPI would actually reflect IDPA (Costantino, Arvidson/Yasaei).

[7] CEDI from currently regulated uses that do not include the EDIs from DMPAs presence as an impurity in other regulated food additives (Costantino, Arvidson/Yasaei, 03/12/2002, RE FCN187, references petition FAP 9B4637 memo of 04/01/1999).

- Pinter Anderson, MEM, and Kara Altshuler, Ph.D., at ICF [Contract No. 223-00-2450, Work Assignment No. 2001-38 (ICF 038)], reviewed the study.
- Conclusion: "Fluorolink PT 5060 was not mutagenic in this bacterial reverse mutation assay in either the absence or presence of exogenous metabolic activation."

In summary, Fluorolink PT5060 did not induce genetic damage under the conditions tested and no information was found in the literature indicating toxic or carcinogenic activity for the polymer. Accordingly, Toxicology has no concerns regarding Fluorolink PT5060 based on its associated exposure and the available toxicity information.

- Impurities:
  - Perfluoroether diol: Two mutagenicity assays conducted using perluoroether diol[8] were submitted in FCN 187 in support of the safety of Fluorolink PT 5060. The reviews of these studies are included as *Attachment 1* to this memo. The conclusions of the submitted studies are provided below.
    - Report #1: Study of the ability of the test article,), to induce gene mutations in strains of *Salmonella typhimurium* and *Escherichia coli.*
      - The study report and data are contained in FCN 187 on pages numbered 274 – 307.
      - Istituto di Ricerche Biomediche, "Antonine Marxer" RBM S.p.A., via Ribes, 1, 10010 – Colleretto Giacosa (Torino), Italy (Bioscience Laboratories & Clinics Group) conducted the study in 1998.
      - Assessment: was not mutagenic or cytotoxic at doses up to 5000 µg/plate, with and without metabolic activation, when evaluated in the bacterial mutation assay.
    - Report #2: Study of the capacity of the test article to induce chromosome aberrations in Chinese hamster ovary cells (CHO).
      - The study report and data are contained in FCN 187 on pages numbered 308 – 341.
      - Istituto di Ricerche Biomediche, "Antoine Marxer" RBM S.p.A., via Ribes, 1, 10010 - Colleretto Giacosa (Torino), Italy (Bioscience Laboratories & Clinics Group) conducted the study in 2001.
      - Results: was not clastogenic at concentrations up to 5000 µg/ml, with and without metabolic activation, when analyzed using CHO cells in this *in vitro* chromosomal aberration study.

In summary, perfluoroether diol did not induce genetic damage under the conditions tested and no information was found in the literature indicating toxic or carcinogenic activity for this impurity. Accordingly, Toxicology has no concerns regarding perfluoroether diol as an impurity in Fluorolink PT5060 based on its associated exposure and the available toxicity information.

  - Isophorone diisocyanate (IPDI): IPDI is negative in the Ames assay when tested with strains TA100, TA1535, TA1537, and TA98 in the presence or absence of metabolic activation (rat or hamster) at doses up to 33 µg/plate[9,10]. RTECS lists the LD_{50} in rats at 4825 mg/kg and cats at 1 mL/kg. Documents in our office include FAP OB3525 and FAP 3B2920 that contain LD_{50} reviews, but no long term or genetic toxicity tests. Although IPDI was inclusive in SAR analysis for carcinogenicity (SAR Team/Yasaei, 01/31/2002, RE FCN187), MCASE analysis for mutagenicity indicates that no biophores were identified in the molecule (Attachment 2, Chanderbhan, 01/09/02). Perusal of the literature and SAR indicates that, unlike IPDI, aromatic ioscynates have a high concern for mutagenicity and carcinogencity. As previously mentioned in this memo, exposure from IPDI may actually be in the form of isophorone diamine (IDPA, CAS No. 2855-13-2). IDPA was recently reviewed by Dr. M. Shackelford (Shackelford/Smith, 11/14/2000, RE FAP 7B4538). IDPA is negative in the Ames assay using strains TA98, TA100, TA1537, and WP 2hcr in the presence or absence of metabolic activation (originally reviewed in Siu/Takeguchi, 10/15/1980, RE FAP 0B3525). A negative finding for the Ames assay using strains TA100 and TA98, in the presence and absence of metabolic

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[8] and. are trade names for perfluoroether diol (Dubeck/Yasaei, 11/21/2001, RE FCN 187, amendment letter).

[9] The notification contained the reference and a data page, full reference was obtained from the CFSAN library for review.

[10] Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B., and Zeiger, E.; Salmonella Mutagenicity Tests: II. Results from the Testing of 270 Chemicals; *Environ. Mutagen.* 8(SUPPL. 7): 1-119, 1986.

activation was found in the public literature[11]. A subchronic toxicity study ("13-week oral toxicity, drinking water, study with IPD in the rat") was reviewed in FAP 8B4118 (Bleiberg/Smith, 08/14/1995). The study was conducted using IPD (Isophorodiamin), which is used interchangeably with IPDA (no other chemical identity information is included). IPD was administered to male and female rats at dose levels of 0.0, 20, 60, or 160 mg/kg/d in drinking water. Due to various effects identified by the reviewer, histophatholically evaluation of the low dose animals was requested prior to the establishment of a NOEL.

IPDI did not induce genetic damage in the Ames assay and SAR and publicly available literature do no indicate a concern for the carcinogenic activity of this impurity. Accordingly, Toxicology has no concerns regarding IPDI as an impurity in Fluorolink PT5060 based on its associated exposure and the available toxicity information.

- 2,2-dimehylol-propionic acid (DMPA): DMPA was recently reviewed by Dr. Chang (Chang/File, 05/24/1999, RE FAP 9B4637). The rat LD_{50} for DMPA is > 10g/kg. SAR analysis using MCASE indicate that the molecule is "not likely to be a potent carcinogen" (SAR Team/Yasaei, 01/31/2002, RE FCN187). A literature search did not produce files indicating carcinogenic or mutagenic concerns for DMPA. According to Chemistry, the EDI of 1.8 µg/p/d is insignificant relative to the CEDI of DMPA from its regulated uses.

Toxicology has no concerns regarding DMPA as an impurity in Fluorolink PT5060 based on its associated exposure and the available toxicity information.

- Dibutyltin dilaurate (DBTDL): Chemistry has estimated the EDI of DBTDL at 0.20 µg/p/d. DBTDL has been determined by the Cancer Assessment Committee (CAC) to be a suspect carcinogen, based on its structural similarity to dibutyltin diacetate (10/18/1979, Ronald J. Lorentzen, Ph.D., Executive Secretary, Meeting of the Cancer Assessment Committee, USFDA). CAC meetings/memorandums on October 18, 1979 and February 1, 1989 conclude, "dietary administration of dibutyltin diacetate is associated with the increase of hepatocellular neoplasms in B6C3F1 mice". Due to the structural similarity of the two compounds and inadequate evidence to the contrary concerning the dilaurate compound, we will assess the safety of the dilaurate compound using the unit cancer risk determined for the diacetate compound [0.014 $(mg/kg\ bw/day)^{-1}$]. Accordingly, the EDI of 0.20 µg/p/d results in a upper bound lifetime cancer risk of 2.6×10^{-8} when the MW of DBTDL is adjusted for DBTDA[12]. This number is approaches two orders of magnitude below the cancer risk considered historically to be of significance[13].

CONCLUSION(S)

Keller and Heckman, on behalf of Ausimont SpA, are notifying to use fluorinated polyurethane anionic resin, prepared by reacting perfluoropolyether diol, isophorone diisocyanate, and 2,2-dimethylolpropionic acid in the manufacturing of paper and paperboard. The final product of use will be a 25-30% aqueous dispersion, Fluorolink PT 5060 (PT 5060 polymer). Ausimont SpA has indicated that the dried resin will be used at levels of less than or equal to 1.5% by weight of the finished dry paper or paperboard, with no food type restrictions and under use conditions B (boiling water sterilized) through H (frozen), as described in Tables 1 and 2 of 21CFR§ 176.170(c), respectively. Based on the EDI of 22 µg/p/d (dietary concentration of 7.2 ppb) for the low molecular weight oligomers of the FCS and the information currently available concerning the toxicity of its impurities, toxicology has no objection to the proposed use of this fluorinated polyurethane anionic resin as described in FCN 187.

Michelle L. Twaroski, Ph.D.
Attachments
Cc: Twaroski, Young, Varner, Adams

[11] Takahashi, A. and Ono, H. Mutagenicity assessment in 44 epoxy resin hardeners in *Salmonella typhimurium* tester strains. *Chem. Epress* 8(9):785-788, 1993.
[12] Costantino, Arvidson/Yasaei, 03/12/2002, RE FCN187
[13] CRC Handbook of Toxicology 1995. Ed.: M.J. Detelanko and M.A. Hollinger. P.656.

000388

FCN 000187

AUSIMONT SpA

SF

Bollate, November 12, 2001

To Devon Hill; Michael Flood
Keller and Heckman LLP

From Giuseppe Malinverno
Ausimont Sp A.

Object: Food Contact Notification

I state that and re different trade names referred to the same product **Perfluoroether diol.**

Giuseppe Malinverno
Head of Regulatory Affairs & Industrial Toxicology
Ausimont S.p A.

000272

Memorandum

Date March 12, 2002

From Division of Food Contact Substance Notification Review
Chemistry Review Group II

Subject FCN 000187 - Ausimont SpA/Keller & Heckman. Submissions dated 10-4-01 and 11-21-01. Fluorinated polyurethane anionic resin as a water and oil repellent used in the manufacture of paper and paperboard.

To Division of Food Contact Substance Notification Review
Regulatory Group II
Attn: P. Yasaei

Keller & Heckman (K&H), on behalf of Ausimont SpA, has submitted this notification for the use of fluorinated polyurethane anionic resin (CAS Reg. No. 328389-91-9) prepared by reacting perfluoropolyether diol (CAS Reg. No. 88645-29-8), isophorone diisocyanate (CAS Reg. No. 4098-71-9), 2,2-dimethylolpropionic acid (CAS Reg. No. 4767-03-7), and triethylamine (CAS Reg. No. 121-44-8) as a water and oil repellent in the manufacture of paper and paperboard. The food-contact substance (FCS) will be used at levels not to exceed 1.5% by weight of the finished dry paper or paperboard that contacts all food types under conditions of use B through H.

Identity and Manufacture

CAS Name: propanoic acid, 3-hydroxy-2-(hydroxymethyl)-2-methyl-, polymers with 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane and reduced Me esters of reduced polymerized oxidized tetrafluoroethylene, compounds with triethylamine

Trade Name: Fluorolink PT 5060,[1] PT 5060 polymer[2]

CAS Reg. No.: 328389-91-9

According to the notifier, the weight average molecular weight (M_w) of the polymer is ~ 21,000 Daltons, and the number average molecular weight (M_n) is ~14,000 Daltons.

[1]Fluorolink PT 5060 is a 25 - 30% aqueous dispersion of the anionic resin.

[2]PT 5060 polymer is the dried anionic polymer.

However, representative gel permeation chromatography (GPC) data from two batches of PT 5060 polymer, provided in Appendix I, show that the M_w = 10,000-14,000 Daltons and the M_n = 5,000-8,000 Daltons.[3] The notifier states that GPC shows that the percentage of the polymer having a molecular weight lower than 1000 Daltons is not more than 0.1 wt-% of the polymer. However, the GPC chromatograms in Appendix I demonstrate that the actual percentage of the polymer having a molecular weight lower than 1000 Daltons is 0.16 wt-%.[4] An infrared spectrum, which supports the structure of the FCS, is provided in Appendix II. A representative structure of the FCS is shown in Appendix III.

The FCS is prepared .

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[3]The notifier mistakenly reported the "Z" average molecular weight (M_z, a higher order average that assigns greater weight to the high-molecular-weight oligomers) as the M_w and the M_w as the M_n.

[4]The 0.16% is actually the average of 0.15% and 0.17% (see Appendix I).

[5]The starting material, PFPED, is manufactured by the notifier as follows. .

The specifications and physical and chemical properties for Fluorolink PT 5060 are provided in Appendix IV. The Material Data Safety Sheets (MSDS) for all the starting materials used to produced the FCS are provided in Appendix VI. The starting materials, which are possible impurities in the FCS, and their CAS Reg. Nos. are listed in Table 1 below.

The specifications for Fluorolink PT 5060 indicate that the combined concentration of the solvents, MEK and IPA, are less than 4% by weight of the dry polymer. When Fluorolink PT 5060 is added at the wet end of the papermaking process, the concentration of the solvents (*i.e.*, MEK, IPA) and TEA in paper would be negligible since all three solvents are water soluble. Any solvent remaining in the paper would be volatilized during steam drying of the paper at 150° C under pressure. If the FCS is added at the size press, any remaining solvent would volatilize during calendering (high-temperature rolling of paper).[6] **Therefore, the exposures to MEK, IPA, and TEA are expected to be essentially zero.**

Use/Technical Effect

The fluorinated polyurethane anionic resin will be used as a water and oil repellant in the manufacture of paper and paperboard. The FCS will be used at levels not to exceed 1.5% by weight of the finished dry paper and paperboard that contacts all food types under conditions of use B through H. Most applications involve the addition of Fluorolink PT 5060 prior to the sheeting forming process; however, it is possible that, for certain applications, the FCS may be added directly at the size press.

The notifier has provided data that demonstrate the oil- and water-repellence properties of the FCS (See page 9 of the FCN). Specifically, the Kit test results demonstrate that, as the amount of FCS in the paper is increased from zero to 1.5% by weight, the oil-repellence of the treated paper reaches its maximum. The $Cobb_{60}$ test results demonstrate that, as the amount of FCS in the paper is increased from zero to 1.5% by weight, the water-absorption of the treated paper reaches it minimum. We concur that the FCS does function as an oil and water repellent.

[6]The boiling points of MEK, IPA, and TEA are 79.6° C (176° F), 82.5° C (180° F), and 89° C (192° F), respectively.

Table 1. Potential Impurities and Their Source		
Starting Material	CAS Reg. No.	Source
IPDI[7]	4098-71-9	monomer
DBTDL[8]	77-58-7	catalyst
PFPED	88645-29-8	"monomer"
MEK[9]	78-93-3	solvent
DMPA[10]	4767-03-7	monomer
TEA[11]	121-44-8	neutralizing agent
IPA[12]	67-63-0	solvent

[7]IPDI (aka 3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate) is regulated as a component of several adhesives under §177.1390 (Laminate structures for use at temperatures of 250° F and above) and as a component of polyurethane resins in contact with bulk quantities of dry food under §177.1680 (Polyurethane resins).

[8]DBTDL is regulated as a catalyst for polyurethane resins under §175.105 (Adhesives) and §177.1680 (Polyurethane resins).

[9]MEK is regulated as a synthetic flavoring substance under §172.515 (Synthetic flavoring substances and adjuvants) and as a solvent in the manufacture of sucrose fatty acid esters under §172.859 (Sucrose fatty acid esters).

[10]DMPA is regulated as a monomer in polyurethane resins used in adhesives under §175.105 (Adhesives) and as a pigment dispersant under §178.3725 (Pigment dispersants).

[11]TEA is regulated as a reactant in the preparation of polyurethane resins used in adhesives under §175.105 (Adhesives) and as an optional adjuvant in the production of polycarbonate resins under §177.1580 (Polycarbonate resins).

[12]IPA is regulated as a synthetic flavoring substance under §172.515 (Synthetic flavoring substances and adjuvants), as a processing aid in the manufacture of modified hop extract under §172.560 (Modified hop extract), and as a residue in spice oleoresins, lemon oil, and hop extracts under §173.240 (Isopropyl alcohol).

Exposure

Low-Molecular-Weight (LMW) Oligomers

The notifier has not performed migration studies. Instead, the notifier calculated the dietary exposure to the LMW oligomers of the dried FCS (aka PT 5060 polymer) using: (1) GPC data from which 100% migration of the LMW oligomers of the PT 5060 polymer (*i.e.*, that fraction having a molecular weight lower than 1000 Daltons) can be calculated, (2) solubility data, and (3) computer modeling. To estimate the dietary exposure, the following assumptions were made:

1. The maximum level of the FCS in paper is 1.5%.

2. Migration of the LMW oligomers (< 1000 Daltons or the soluble fraction) of the PT 5060 into food is 100% from paper having a basis weight of 50 mg/in^2.

3. Ten grams of food contacts each in^2 of paper.

4. The consumption factor CF for coated paper is 0.2.[13]

Since we prefer experimental (actual) data over modeling data and there is not enough information provided in the notification to allow us to adequately evaluate the computer model, we will evaluate only the dietary exposure estimates calculated using the GPC and solubility data.

Using GPC Data

As previously stated in the Identity and Manufacture section above (see footnote 3), the percentage of PT 5060 polymer having a molecular weight below 1000 Daltons is 0.16 wt-%. Using this value and the other assumptions listed above, we calculated the concentration in food (<M>) and dietary concentration (DC) of the LMW oligomers of PT 5060 polymer as follows:

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[13]The notifier stated that the CF for uncoated paper is 0.10 and used that CF to calculate the dietary exposure. However, we have used the CF for coated paper when calculating the dietary exposure to oil and water repellents on food-contact paper (see the chemistry memoranda dated 9-28-93 concerning FAP 3B4353 written by S. Carberry, dated 8-30-96 concerning FAP 6B4513 written by M. VanDerveer, and dated 3-7-00 concerning FAP 0B4719 written by R. Costantino).

<M> = 0.16 g oligomers/100 g FCS x 1.5 g FCS/100 g paper x 0.050 g paper/in^2 paper x

in^2 paper/10 g food = 0.12 mg oligomer/kg food

DC = CF x <M> = 0.2 x 0.12 mg/kg = 0.024 mg/kg or 24 ppb

Based on a daily diet of 3000 g food/person/day, the estimated daily intake (EDI) would be 72 µg/p/d (24 x 10^{-9} g oligomers/g food x 3000 g food/p/d = 72 µg/p/d).

Using Solubility Data

The notifier has determined the solubility of PT 5060 polymer by heating three samples in olive oil at 80° C for 15 hours. After equilibration at room temperature for several hours, aliquots of each sample were analyzed by ^{19}F nuclear magnetic resonance spectrometry (NMR) to determine the level of oligomers.[14]

The sample resulting in the highest solubility had a concentration of oligomer in olive oil of 118 mg oligomer/kg olive oil, which is equivalent to 0.0486 wt-% of PT 5060 extracted.[15] Using this value and the other assumptions listed above, the concentration in food (<M>) and dietary concentration (DC) of the LMW oligomers of PT 5060 polymer is calculated below.

<M> = 0.0486 g oligomer/100 g FCS x 1.5 g PT FCS/100 g paper x

0.050 g paper/in^2 paper x in^2 paper/10 g food = 0.036 mg oligomer/kg food

DC = 0.2 x 0.036 mg/kg = 0.0072 mg/kg or 7.2 ppb

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[14]In Appendix VII, the method used to determine the level of oligomers, the calibration curve, standard and sample spectra, and validation procedure were provided. Fluorolink PT 5060 was used in the standard calibration solutions to construct the calibration curve of the a/b ratio [integrated signals of -67.5 ppm (b)/-89.0 ppm (a)] versus the mg PT5060/kg solvent using an inner tube solution of 1,2-difluorotetrachloroethane as the internal standard. The validation procedure consisted of spiking a blank olive oil sample with 194 mg/kg of PFPED, a polymeric starting material that is similar in structure to the oligomers. This spike was at approximately the detected level of the oligomers (118 - 149 mg/kg). The percent recovery was 97.4%. The notifier states that NMR spectroscopy is an intrinsically quantitative technique and does not require additional calibration.

[15][(118 mg oligomer/kg olive oil x 2.09 x 10^{-3} kg olive oil) ÷ 507 mg PT 5060] = 0.000486 x 100 = 0.0486 wt-% of the polymer is extracted.

Based on a daily diet of 3000 g food/p/d, the EDI of oligomers from use of the FCS is 22 μg/p/d (7.2 x 10^{-9} g oligomers/g food x 3000 g food/p/d = 22 μg/p/d).

The exposure to the LMW oligomers, as determined by 100% migration of the LMW fraction (< 1000 Daltons) of the FCS (24 ppb DC), is very conservative. Solubility data for the FCS result in a more realistic dietary exposure to the LMW oligomers (7.2 ppb DC). We therefore accept 7.2 ppb DC (22 μg/p/d EDI) as the exposure to the LMW oligomers of the FCS.

Starting Materials and Impurities

Dibutyltin dilaurate (DBTDL)

, the EDI becomes:

= 0.20 μg DBTDL/p/d

The corresponding DC is 0.067 ppb (0.20 μg DBTDL/p/d ÷ 3000 g food/p/d = 0.067 μg DBTDL/kg food).

Perfluoropolyether diol (PFPED)

The solubility data described above for LMW oligomers include PFPED, a polymeric starting material (considered one of the starting "monomers") having a M_w of ~2000 Daltons and M_n of ~1500 Daltons. The dietary exposure to PFPED from the intended use of the FCS would be only a fraction of the dietary exposure to the LMW oligomers (7.2 ppb in the diet) from the use of the FCS. Therefore, a very conservative estimate of the dietary exposure to PFPED from the use of the FCS would be < 7.2 ppb in the diet or 22 μg/p/d.

Isophorone Diisocyanate (IPDI) and 2,2-Dimethylolpropionic Acid (DMPA)

Unlike the catalyst and oligomers, IPDI and DMPA are not substantive to paper pulp and are highly water-soluble. Their potential concentrations in food may be obtained using standard calculations based on wet-end additive dilutions.

The assumptions are:

1. White slurry water in the head box consists of 0.6% fiber in the aqueous solution.

2. Wet paper that has been sheet-formed but not steam-dried consists of 33% fiber and 67% water. Since the additive is not substantive to paper, the mass of water (containing the additive) in contact with pulp at the point in the papermaking process where the slurry enters the dryers determines the level of additive retained in the paper.

3. After drying, the finished paper contains approximately 92% fiber and 8% water.

4. Any compound present after sheet forming remains in the finished paper on steam drying.

5. The basis weight of paper is 0.05 g/in^2.[21]

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[21]In a memorandum of meeting dated 4-13-95 written by Allan Bailey, it was determined that the average basis weight of paper for these types of calculations would be 50 mg/in^2. This conclusion was supported by the observation that food-contact paper and paperboard basis

6. Migration of the each compound into food from the finished paper is 100%.

7. Ten grams of food contacts each in^2 of paper.

As an example, the <M> of IPDI is calculated below.[22] IPDI is present in the FCS at 0.21 wt-%,[23] and the FCS is added at the wet end at 1.5% by weight/g paper. Using assumptions 1 and 3, we calculate the IPDI in the water slurry for coated paper (see footnote 12) to be:

0.21 g IPDI/100 g FCS x 1.5 g FCS/100 g paper x 100 g paper/92 g fiber x

0.6 g fiber/100 g slurry = 0.20 μg IPDI/g slurry

Using assumptions 2 and 3, we calculate the concentration of IPDI in the finished paper to be:

0.20 μg IPDI/g slurry x 67 g slurry/33 g fiber x 92 g fiber/100 g paper

= 0.37 μg IPDI/g paper

Using assumptions 5 - 7, we calculated the concentration of IPDI in food (<M>) to be:

0.37 μg IPDI/g paper x 0.050 g paper/in^2 paper x in^2 paper/10 g food

= 1.9 ng IPDI/g food or 0.0019 mg IPDI/kg food

Using a CF of 0.2, the DC of IPDI from the proposed use of the FCS is:

DC = CF x <M> = 0.2 x 0.0019 mg IPDI/kg food = 0.38 ppb

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weighs range from 20 - 100 mg/in^2.

[22]IPDI readily hydrolyzes to isophorone diamine (IPDA; aka 5-amino-1,3,3-trimethyl-cyclohexanemethylamine) in the presence of water. Therefore, if any residual IPDI remains during the manufacture of the FCS it would be hydrolyzed to IPDA when water is added in the last step prior to distillation. So the <M> of IDPI would actually reflect the <M> of IPDA.

[23]This assumes that IDPI represents 21% by weight of the total monomers in the FCS and that 1% of the IDPI remains free in solution unreacted (see p. 17 of the FCN).

The EDI of IPDI from the use of the FCS, based on a 3000 g food/p/d, is:

$$EDI = 3000 \text{ g food/p/d} \times 0.38 \times 10^{-9} \text{ g IPDI/g food} = 1.1 \text{ µg IPDI/p/d}$$

The DC and EDI of DMPA are calculated similarly and are tabulated below. For convenience, the exposure estimates to the other two starting materials, calculated previously in this memorandum, are also included in the table.

Table 2. Exposure to Starting Materials

Compound	Wt-% in the FCS	DC	EDI
IPDI	0.21	0.38 ppb	1.1 µg/p/d
DMPA[24]	0.33	0.6 ppb	1.8 µg/p/d
DBTDL	.	0.067 ppb	0.20 µg/p/d
PFPED		< 7.2 ppb	22 µg/p/d

Cumulative Exposure to DMPA

The cumulative exposure to DMPA from its currently regulated uses is 38 ppb DC or 0.11 mg/p/d (see our chemistry memorandum dated 4-1-99 concerning FAP 9B4637). A table summarizing DMPA's regulated uses and their contributions to the cumulative exposure to DMPA is provided in Table 3 below.

The cumulative exposure to DMPA as an impurity in other regulated food additive uses cannot be calculated because additional data on the levels of residual DMPA in food additives in which DMPA may be present are not available. However, the EDI of DMPA as an impurity in the FCS was calculated to be 1.8 µg/p/d (0.6 ppb DC). This value is insignificant relative to the EDI to DMPA from its currently regulated uses (0.11 mg/p/d).

[24]This assumes that DMPA represents 6.5% by weight of the total monomers in the FCS and that 5% of the DMPA remains in solution unreacted (see p. 17 of the FCN).

Table 3. Cumulative Exposure to DMPA from Its Regulated Uses			
Regulation	Use	DC	EDI
Indirect Additive Uses			
§175.105	as a monomer in polyurethane resins used in adhesives	7.0 ppb	21 μg/p/d
§178.3725	as a pigment dispersant	6.6 ppb	20 μg/p/d
Presence as a Constituent			
§176.170	as a residual monomer in the production of anionic polyurethane resin used as a surface sizing agent in paper and paperboard	4.2 ppb	13 μg/p/d
§176.170	as a residual monomer in the production of polyester resin used as surface sizing agent in paper and paperboard	20 ppb	60 μg/p/d
TOTAL		**38 ppb**	**0.11 mg/p/d**

Cumulative Exposure to DBTDL

The cumulative exposure to DBTDL has not been determined. (Currently, there are two regulations that permit the use of the catalyst in the formation of polyurethane resins used in adhesives (§175.105) and in bulk food containers used in contact with dry foods only (§177.1680).) There are probably many other instances in which DBTDL or other dibutyltin catalysts are present as impurities in other regulated food additives. However, a preliminary investigation of FAPs in which dibutyltin catalysts were included in the manufacturing processes for regulated additives has shown that the data needed to calculate exposure to the catalysts are not available. The EDI of DBTDL as an impurity in the FCS is 0.20 μg/p/d (0.067 ppb DC). This value is probably insignificant relative to the cumulative EDI from the regulated uses of dibutyltin catalysts and their presence as impurities in other regulated food additives.

Risk Assessment for DBTDL

Previously, the Cancer Assessment Committee (CAC) determined a carcinogenic unit risk for dibutyltin diacetate (DBTDA; a compound similar in structure to DBTDL) of

0.014 (mg/kg bw/d)$^{-1}$.[25] After adjusting the EDI of DBTDL for the differences in molecular weight of DBTDL and DBTDA, the EDI becomes:

$$0.20\ \mu g\ DBTDL/p/d \div 631.6\ g\ DBTDL/mol\ DBTDL = 3.17\times10^{-10}\ mol\ DBTDL/p/d$$

$$3.17\times10^{-10}\ mol\ DBTDL/p/d = 3.17\times10^{-10}\ mol\ DBTDA/p/d$$

$$3.17\times10^{-10}\ mol\ DBTDA/p/d \times 351.0\ g\ DBTDA/mol\ DBTDA =$$

$$= 0.111\ \mu g\ DBTDA/p/d$$

By multiplying the EDI of the carcinogen (in mg/kg bw/d) by its unit risk [in (mg/kg bw/d)$^{-1}$], the upper bound risk for that carcinogen may be determined. The calculation follows:

$$0.111\ \mu g/person/d\ \times\ person/60\ kg\ bw = 1.85 \times 10^{-9}\ g/kg\ bw/d$$

$$1.85 \times 10^{-6}\ mg/kg\ bw/d \times 0.014\ (mg/kg\ bw/d)^{-1} = 2.6 \times 10^{-8}$$

Notification Language

The acknowledgment letter dated 10-28-01 was appropriate as corrected and signed off on 12-3-01.

Summary

We have no questions.

K. Paquette for
Roseann M. Costantino, Ph.D.

Kirk B. Arvidson, Ph.D.

[25]CAC determined the carcinogenic unit risk for DBTDA in its report dated 5-23-83.

SOLVAY SPECIALTY FCN 195

C. CHEMICAL IDENTITY OF FOOD CONTACT SUBSTANCE

Fluorolink® F10 is the phosphate ester of ethoxylated perfluoroether diol.

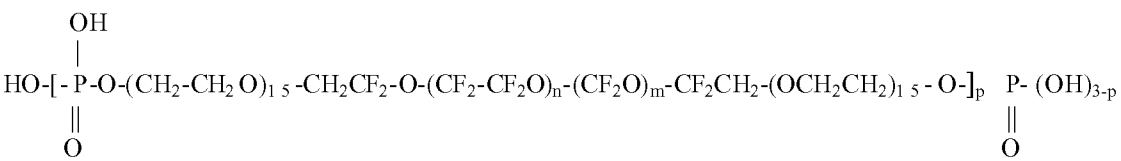
Chemical Abstracts Name:	Diphosphoric acid, polymers with ethoxylated reduced Me esters of reduced polymd. oxidized tetrafluoroethylene
Chemical Abstracts Reg. No.:	200013-65-6

The polymer is prepared in two steps:

1. Perfluoroether diol is reacted with ethylene oxide.
2. The ethoxylated perfloroether diol is reacted with either phosphorous pentoxide or pyrophosphoric acid to form the phosphate ester.

The complete manufacturing process, including the manufacturing process for the perfluoroether diol, is provided in Appendix I (Confidential).

Fluorolink® F10 is a mixture of mono- and diphosphate esters. A representation of the structure would be the following:



where p = 1 for the monoester and p = 2 for the diester, and n and m are about 6.

The diphosphate ester results from the reaction of two acidic groups of the pyrophosphoric acid with the ethoxylated perfluoroether diol. Due to the polyfunctional

phosphorus reagent, either phosphorus pentoxide or pyrophoric acid, a mixture of products cannot be avoided. In Fluorolink® F10 the diester is typically present at levels of up to 30 mole percent.

Fluorolink® F10 in its acid form is not soluble in water. In order to apply the product onto the paper, it is necessary to partially neutralize the acid with ammonia. The pH of the solution, as applied to the paper, is about 7[1]

Typical properties of Fluorolink® F10 are shown in the following table:

Functional Groups	Phosphate
Color	Pale brown
Appearance	Viscous liquid
Specific Gravity (20°C)	1.73 g/cm^3
Dynamic Viscosity (20°C)	60,000 cps
Solubility at 25°C	
Water	Insoluble
Isopropyl Alcohol	≤ 0.5 wt. %
n-Hexane	Insoluble
Toluene	Insoluble
Propylene Glycol	≤ 0.5 wt. %
Acetone	Insoluble
Methyl Ethyl Ketone	Insoluble

The infrared spectrum of Fluorolink® F10 and a gel permeation chromatogram (GPC) for ethoxylated perfluoroether diol are provided in Appendix II. The weight average molecular weight is about 1800 daltons; the number average molecular weight is about 2200 daltons. The molecular weight distribution of Fluorolink® F10 will only be slightly higher than that of the ethoxylated perfluoroether diol.

[1] As reported in Section F of this Notification, paper samples used in the migration testing, were prepared using both partially neutralized and completely neutralized Fluorolink® F10.

Material Safety Data Sheets (MSDS) for the starting materials, and specification sheets for ethoxylated perfluoroether diol and perfluoroether diol, the precursor to ethoxylated perfluoroether diol, are provided in Appendix III.

Impurities

Perfluoroether diol is completely converted to the ethoxylate, and will not be present in Fluorolink® F10 in any appreciable concentration. Ethoxylated perfluoroether diol may be present in Fluorolink® F10 at up to 5 wt.%.

Other impurities may include phosphoric acid, up to 1%; isobutyl alcohol, up to 0.3%; ethanol, up to 0.1%; and acetic acid, at levels up to 0.2%. Phosphoric acid, ethanol and acetic acid are GRAS food substances (21 C.F.R. § 182.1073, § 184.1005 and § 184.1293, respectively) and will not be discussed further in this Notification.

Since and ethylene oxide (EO) are used in the manufacturing process of Fluorolink® F10, precursors to Fluorolink® F10 were analyzed for EO, and 1,4-dioxane. TFE

EO and 1,4-dioxane were not detected in ethoxylated perfluoroether diol at detection limits of 0.24 part per million (ppm) and 1.6 ppm, respectively. Complete reports are provided in Appendix IV.

D. INTENDED CONDITIONS OF USE

Paper treated with Fluorolink® F10 may be used in contact with all types of food under Conditions of Use C through H, as set forth in 21 C.F.R. § 176.170(c), Table 2.

Fluorolink® F10 may be added prior to sheet forming or at the size press during the manufacture of paper and paperboard in order to impart oil and water repellence. The maximum addition level of Fluorolink® F10 is 1.5% by weight of dry finished paper or paperboard. The polymer is fully substantive to the paper fibers.

E. INTENDED TECHNICAL EFFECT

- imparts oil and water resistance to paper and paperboard.

Oil- and water-repellence properties are measured, respectively, through the Kit Test (TAPPI method 557) and the $Cobb_{60}$ test for water adsorption (TAPPI method T441). Typical properties of the paper treated with increasing levels of

are shown in the following table:

Percent Weight F10 in Paper	Kit Test Value	$Cobb_{60}$ Test Value (g/m^2)
0	0	110
0.3	5	95
1.0	9	72
1.5	10	65

F. ESTIMATED DAILY INTAKE (EDI)

1. Fluorolink® F10 Oligomers

Migration testing on paper treated with Fluorolink® F10 was performed by TNO Nutrition and Food Research Institute. The complete report is provided in Appendix IV.

Eight different paper samples were tested, in addition to blank paper:

1. Paper in which Fluorolink® F10 was added to pulp (wet end preparation). Two different samples were prepared – one using the most neutralized product; the other using the least neutralized product. Paper samples were prepared using Fluorolink® F10 levels of 0.5% and 1.5%.

2. Paper treated with Fluorolink® F10 at the size press. Again, four different samples were prepared reflecting different degrees of neutralization, and Fluorolink® F10 use levels of 0.5% and 1.5%.

Paper was extracted with 10% ethanol, 50% ethanol, or *n*-heptane for 2 hours at 100°C. Extraction under these conditions would support FDA's "Condition of Use H," 21 C.F.R. § 176.170(c), Table 2.[2] However, the results should also support Condition of Use C (hot filled or pasteurized at temperatures above 66°C).

Samples were analyzed by an LC-MS procedure described in Appendix IV. Fluorolink® F10 was not found in any of the extracts from samples treated at the wet end at a level corresponding to 0.27 • g/in^2 (27 ppb in food) in the 10% or 50% ethanol extracts. With samples added at the size press, no migration was observed in 10% ethanol, but apparent migration, corresponding to about 50 ppb in food, was observed in

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[2] Guidance for Industry, Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations, FDA, Center for Food Safety and Applied Nutrition, September, 1999 (revision 1.1, May, 2000), page 21 of 35.

50% ethanol. The investigators noted that the LC-MS spectrum was very similar to that from the 50% ethanol extraction on blank paper.[3] Hence, after consultation with Keller and Heckman LLP it was decided to repeat the migration testing using *n*-heptane, a more realistic fatty food simulant for paper products than 50% ethanol, an extremely aggressive solvent for paper. Using heptane as a food simulant, no Fluorolink® F10 was detected at a level of 0.22 • g/in^2.

Analyses were validated by spiking extracts at a level corresponding to 0.50 • g/in^2. Average percent recoveries varied from 92-116 percent, with excellent precision (Tables 8-10 of TNO report). Validation was repeated using a lower spiking level, corresponding to 0.26 • g/in^2, (Addendum, dated September 21, 2000, to TNO report, Appendix IV). Percent recoveries varied from 87±4% to 95±6%.

Dietary Concentration and EDI for Fluorolink® F10 Oligomers

Using the detection limits of 27 ppb for aqueous and alcoholic foods and 22 ppb for fatty foods with the consumption factor and food distribution factors for uncoated paper, the dietary concentration of Fluorolink® F10 oligomers is:

CF<M> = 0.10 x [(0.59) x (27 ppb) + (0.41) x (22 ppb)] = **2.5 ppb**

Based on total food consumption of 3 kg/person/day (kg/p/d), the EDI would be **7.5 • g/p/d**.

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[3] The LC-MS chromatogram and mass spectrum of a Fluorolink® F10 standard is shown in Figure 21 of the TNO report. The mass spectrum is qualitatively different from that from the 50% ethanol blank extraction, shown in Figure 13.

2. Ethoxylated Perfluoroether Diol

Unreacted ethoxylated perfluoroether diol may be present in Fluorolink® F10 at levels up to about 5%. Since the molecular weight is similar to the product, the migration characteristics of the ethoxylated perfluoroether diol should be similar, *i.e.* little migration is expected. Moreover, the LC-MS method used in the analysis of Fluorolink® F10 in extracts from treated paper would also quantitate the precursor. We conclude that the maximum concentration of the ethoxylated perfluoroether diol will be no higher than that of Fluorolink® F10 itself, and will almost certainly be much lower.

3. Isobutyl Alcohol (IBA)

IBA, a solvent employed in the manufacture of Fluorolink® F10, may be present in the product at a maximum 0.3%. If this entire quantity remains in the paper with Fluorolink® F10 and subsequently migrates into food, the concentration in food would be 0.2 ppm, and dietary exposure would be 20 ppb.[4] However, it is expected that little, if any, of this solvent will be present in finished paper subsequent to the final heating to remove water.

[4] $(0.015\ g_{product}/g_{paper})(0.003\ g_{IBA}/g_{product})(0.050\ g_{paper}/in^2)/(10\ g_{food}/in^2) = 2 \times 10^{-7}\ g_{IBA}/g_{food}$, or 0.2 ppm.

5. Ethylene Oxide and 1,4-Dioxane

Ethylene oxide and 1,4-dioxane were not found in a Fluorolink® F10 precursor at levels of 0.24 ppm and 1.6 ppm, respectively. Using the same assumptions as for TFE, maximum potential dietary concentrations of these two substances are **1.8 ppt for ethylene oxide and 12 ppt for 1,4-dioxane**. The EDI for ethylene oxide and 1,4-dioxane would be no higher than **5.4 ng/p/d and 36 ng/p/day**, respectively.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: February 11, 2002

From: Division of Food Contact Substance Notification Review, Chemistry Review Group 1

Subject: FCN 195: Ausimont SpA; Notification for the use of phosphate esters of ethoxylated perfluoroether as a water and oil repellent in the manufacture of paper and paperboard. Submissions dated 11/6/2001, and 12/19/2001.

To: Division of Food Contact Substance Notification Review, Regulatory Group 1
Attn.: A. Shanklin, Ph.D.

Ausimont SpA, through their agent Keller and Heckman LLP (K&H), have submitted a notification for the use of the food contact substance (FCS) identified as phosphate esters of ethoxylated perfluoroether, prepared by reaction of ethoxylated perfluoroether diol (EPFED) with phosphorous pentoxide or pyrophosphoric acid, for use as a water and oil repellent in the manufacture of paper and paperboard at a level not to exceed 1.5% by weight in the finished paper and paperboard. The FCS is currently not regulated nor is the subject of any effective notifications.

Identity

Information concerning the identity of the FCS is included in Section C of the FCN (pp. 5-7).

FCS Name: phosphate esters of ethoxylated perfluoroether prepared by reaction of ethoxylated perfluoroether diol (CAS Reg. No. 162492-15-1) with phosphorous pentoxide (CAS Reg. No. 1314-56-3) or pyrophosphoric acid (CAS Reg. No. 2466-09-3).

CAS Reg. No.: 200013-65-6

CAS Name: Diphosphoric acid, polymers with ethoxylated reduced Me esters of reduced polymerized oxidized tetrafluoroethylene

Trade Name: Fluorolink F10

Weight average molecular weight: ·99999999999

Number average molecular weight: 999999999999

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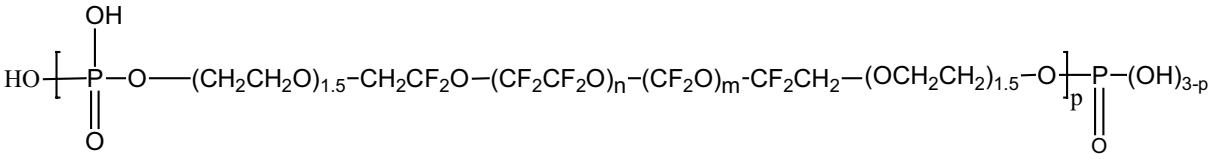
Structure:



-where p=1 for the monoester, and p=2 for the diester (the diester is present at levels up to 30 mole percent)
-values for n and m are approximately 6

Fluorolink F10 Properties

Table 1. Summary of Physical and Chemical Properties

Property	**Value**
Functional groups	Phosphate
Color	Pale brown
Appearance	Viscous liquid
Specific gravity (20º C)	1.73 g/cm^3
Dynamic viscosity (20º C)	60,000 cps
Solubility at 25º C	
Water	Insoluble
Isopropyl alcohol	Ω0.5 wt.%
n-hexane	Insoluble
Toluene	Insoluble
Propylene glycol	Ω0.5 wt.%
Acetone	Insoluble
Methyl ethyl ketone	Insoluble

Characterization

Spectral data identifying the FCS is included in Appendix II of the FCN. The notifier included an infrared (IR) spectrum of Fluorolink F10 as well as a gel permeation chromatogram (GPC) for EPFED, a precursor of the FCS. The peak at about 1250 cm^{-1} in the IR spectrum may be attributed to the stretching of the P-O double bond (P=O). The data are consistent with the molecular structure given, and adequately characterize the FCS.

We have no questions on the identity of the FCS.

Manufacture

Information concerning the manufacture of the FCS is included on page 5 of the FCN, as well as in Appendix I (description of manufacturing process) and Appendix III (information on starting materials and precursors). The FCS is manufactured in three separate processes. The

EPFED (II)

EPFED is manufactured via a two step process. PFED (1700 kg) and potassium *tert*-butoxide (13 kg) are mixed and heated to 80°C in a 3000 L vessel. Ethylene oxide (EO) is then added to the mixture over an 8 hour period during which time the contents are maintained at 80°C. Nitrogen is then sparged through the reaction mixture for 5 hours at 80°C in order to remove unreacted EO and *tert*-butyl alcohol (TBA). Next, the product is washed with a mixture of water (9350 kg) and isobutyl alcohol (105 kg). The organic phase is then separated and acidified by addition of hydrochloric acid. Finally, the excess acid and traces of isobutyl alcohol are removed by evaporation to yield EPFED (II) as shown below.

$$HO—(CH_2CH_2O)_{1.5}-CH_2CF_2O—(CF_2CF_2O)_n—(CF_2O)_m-CF_2CH_2—(OCH_2CH_2)_{1.5}—OH \quad \text{(II)}$$

Phosphate esters of ethoxylated perfluoroether

The FCS is manufactured by means of a three step process. EPFED (700 kg), water (15 kg), and phosphorous pentoxide (P_2O_5, 98 kg)[2] are combined and heated at 90°C for 8 hours in a 2000 L vessel. The reaction mixture is cooled to 40°C and diluted with ethyl acetate (280 kg). Water (840 kg) is then added to the reaction vessel, and the mixture is stirred for 1 hour at 40°C. Next, the aqueous and organic phases are allowed to separate for a period of 3-4 hours.

[2]Or an equivalent amount of pyrophosphoric acid ($P_2O_7H_4$) may be used.

The organic phase is then collected and isobutyl alcohol (200 kg) is added. Finally, the organic solvent and water are removed by vacuum distillation to yield the FCS.[3]

Impurities

Information on i‹··)9999es in the FCS is discussed in Section C (p.7) of the notification. Residue levels fo999999 EO and 1,4-dioxane (see Appendix IV) were determined by analysis of the polymer precursor, EPFED (see II), not the FCS. 1,4-Dioxane and EO were extracted using dimethylacetamide followed by analysis using gas chromatography-mass spectrometry (GC-MS). ··)999 was analyzed by means of head space analysis and gas chromatography employing a flame ionization detector (GC-FID).

Table 2. Impurity Composition

Impurity	CAS #	Residual Level
EPFED	162492-15-1	Up to 5 wt-%
Isobutyl alcohol (solvent)	78-83-1	0.3 wt-%
Phosphoric acid	7664-38-2	Up to 1 wt-%
Ethanol	64-17-5	Up to 0.1 wt-%
Acetic acid	64-19-7	Up to 0.2 wt-%
·99999999999 999999999	999999999999999999999999999999999999	
Ethylene oxide (EO)	75-21-8	< 240 ppb (residual level in precursor)
1,4-dioxane	123-91-1	< 1.6 ppm (residual level in precursor)

Phosphoric acid, ethanol, and acetic acid are claimed by the notifier to be generally recognized as safe (GRAS) under 21 CFR 182.1073, §184.1293, and §184.1005, respectively. The notifier claims that PFED would not be present in the FCS since all PFED would be converted to EPFED during the manufacturing process (p.7). Phosphorous pentoxide and pyrophosphoric acid would not be expected to be present in the FCS since these species would rapidly convert to phosphoric acid in the presence of water.

We have no questions on the manufacture of the FCS.

Use Level and Intended Technical Effect

Information concerning the use level for the FCS is included in Section D (p. 8). The FCS is intended to impart oil and water repellence to food-contact paper and paperboard. The FCS will be added to paper and paperboard, at either the wet-end or at the size press, at a level not to exceed 1.5% by weight in the finished paper and paperboard. Paper treated with the FCS

[3]The final two steps of the manufacturing process are described in Appendix I as phase separation and distillation processes. The actual methodological description of the final two steps is somewhat vague, however, this is not deemed to be critical enough of an issue to attain comment from the notifier.

will be used in contact with all food types under Conditions of Use C through H, as set forth in 21 CFR 176.170(c), Table 2.

The intended technical effect is discussed in Section E (p. 9). Results from two tests designed to determine oil (the Kit Test, TAPPI method 557) and water repellency (the Cobb60 test, TAPPI method T441) are included. The test results indicate increased oil or water repellence in paper as the use level was increased from 0 to 1.5 wt-% in paper.

We have no questions on the use and intended technical effect of the FCS.

Migration and Extraction Studies

Both migration and extraction studies, which were conducted by TNO Nutrition and Food Research Institute, are summarized in Section F of the FCN (pp. 10-13) and detailed in Appendix IV. Appendix IV presents the procedure and results for the extraction studies in Sections 2.2 and 3.1, respectively, and the procedure and results for the migration studies in Sections 2.3 and 3.2, respectively.

Comment on Migration Protocol

Migration tests for the FCS were conducted on paper samples containing the FCS for 2 hours at 100°C in 10% ethanol, 50% ethanol, and n-heptane. According to our Chemistry Guidance document, this migration protocol is suitable for Condition of Use H. The notifier, however, has requested Conditions of Use C through H. Our recommendations for Condition of Use C are to carry out migration studies at 100°C for 30 minutes followed by 40°C for 238 hours, or alternatively, 66°C for 2 hours followed by 40°C for 238 hours. We asked the notifier to present us with the rationale for use of the Condition of Use H migration protocol (100°C for 2 hours) to cover Condition of Use C. The notifier submitted this argument as part of the 12/19/2001 submission. The notifier performed a simple diffusion calculation using the equation[4]:

$$M_t \mid 2\Delta C_{p0} \Delta \psi \Delta \left(\frac{D_p t}{\pi \phi} \right)^{1/2}$$

Where M_t is migration at time t, C_{p0} is the initial concentration of the migrant in the polymer[5], ψ is the density of the polymer, and D_p is the diffusion coefficient of the migrant in the

[4]Crank, J. *The Mathematics of Diffusion*, Clarendon Press: Oxford, UK, 1975.

[5]While the main substrate in the migration testing is paper, the notifier is considering migration of oligomers of the FCS from the main polymeric FCS. In reality, the FCS is imbedded in or on paper, but by using this equation the notifier is making the conservative estimate of migration from a polymer film of the FCS having infinite thickness.

polymer. Diffusion coefficients for 150 and 500 dalton oligomers of the FCS were determined using the following equation[6]:

$$D_p \mid 10^4 \Delta \exp(A_p 4 a \Delta M_r 4 b \Delta T^{41})$$

Where D_p is the diffusion coefficient, A_p is a factor accounting for the effect of the polymer on diffusivity, M_r is the molecular weight of the substance, T is the temperature in degrees Kelvin, and *a* and *b* are correlation constants for molecular weight and temperature effects on diffusion with values of 0.01 and 10450, respectively.[7] Using the above equation, the notifier determined diffusion coefficients at temperatures of 100∀C, 66∀C and 40∀C for the oligomers of the FCS having molecular weights of 150 and 500 daltons.[8] Using these values they were able to determine representative migration values for the three migration protocols of interest. These are tabulated below from the notifier's Table 2 in the 12/19/2001 submission.

Table 3. Summary of Estimated Migration Values for Oligomers

Migration Protocol	**150 Dalton Oligomers**	**500 Dalton Oligomers**
100∀C for 2 hrs.	0.24 ppm	0.042 ppm
100∀C for 30 minutes + 40∀C for 240 hrs.	0.30 ppm	0.052 ppm
66∀C for 2 hours + 40∀C for 240 hrs.	0.24 ppm	0.041 ppm

Based on the calculated representative migration values for the different protocols, the notifier argued that migration values obtained using Conditions of Use H (100∀C for 2 hours) would <u>not</u> differ significantly from those obtained using FDA's recommended protocol for Condition of Use C (66∀C for 2 hours + 40∀C for 238 hours). As a result, for this notification, we will accept their migration protocol of 100∀C for 2 hours to allow for Conditions of Use C through H. We have no objections to the notifier's approach.

<u>FCS</u>

Migration tests for oligomers of the FCS were performed for 2 hours at 100∀C in 10% ethanol, 50% ethanol, and n-heptane on eight different paper samples comprised of the following two groups:

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[6] Baner, A., Brandsch, J., Franz, R. and Piringer, O. (1996). The application of a predictive migration model for evaluating the compliance of plastic materials with European food regulations. *Food Additives and Contaminants* **13(5),** 587-601.

[7]The submission from the notifier contains an error regarding the value of the constant *a*. The value for *a* is 0.01, not 0.1 as contained in the notifier's amendment.

[8]While the notifier employed the correct diffusion coefficients when they calculated migration, they listed incorrect diffusion coefficient values in their Table 1 for the 150 dalton oligomer at all three temperatures. The actual diffusion coefficient values are: for 100∀C, 1.5×10^{-9} cm^2/sec; for 66∀C, 9.3×10^{-11} cm^2/sec; and for 40∀C, 7.2×10^{-12} cm^2/sec.

1.) Four test samples consisting of paper in which the FCS was added to pulp at the wet-end of paper manufacture. The samples contained either 0.5 wt-% or 1.5 wt-% of the FCS, and were manufactured from a completely neutralized version and a partially neutralized version of the FCS.[9] These samples are denoted as wet-end addition (WEA).

2.) Four test samples consisting of paper that was treated with the FCS at the size press. The samples contained either 0.5 wt-% or 1.5 wt-% of the FCS, and were manufactured from a completely neutralized version and a partially neutralized version of the FCS.[9] These samples are denoted as size press addition (SPA).

From each of the paper samples, a test specimen measuring 10 x 15 cm (23.25 in^2) was cut into about 1 cm^2 pieces and transferred to a vial to which 40 ml of the food simulant was added. The 10% ethanol food simulant was used to simulate migration to aqueous, acidic and low alcoholic food types. Both 50% ethanol and n-heptane were used to simulate migration to fatty foods. The vials were then placed in an oven at 100∀C for 2 hours. Upon completion of the 2 hour time period, the remaining paper was filtered and the vial washed with methanol. The food simulant and the methanol wash were combined and evaporated using nitrogen. The residue was dissolved in isopropanol (0.5 ml) and analyzed for the presence of the FCS using liquid chromatography-mass spectrometry (LC-MS) over a mass-to-charge (m/z) range of 900 to 1700 daltons (as described in Appendix II of TNO's report contained in Appendix IV of the FCN). Quantification of the FCS was performed by means of an external standard calibration.

Since the use level of the FCS will be up to 1.5 wt-% in food, we will only consider migration from paper containing the FCS at the 1.5 wt-% level. Tables 3 and 4 below show data taken from Tables 4 and 5 of Appendix IV.

Table 4. Migration of the FCS into 10% ethanol.

Paper Sample	**Migration from Paper**	**Migration into Food[10]**
Wet End Addition (WEA), partially neutralized, 1.5 wt-% FCS	< 0.27 σg/in^2	< 27 σg/kg
WEA, completely neutralized, 1.5 wt-% FCS	< 0.27 σg/in^2	< 27 σg/kg
Size Press Addition (SPA), partially neutralized, 1.5 wt-% FCS	< 0.27 σg/in^2	< 27 σg/kg
SPA, completely neutralized, 1.5 wt-% FCS	< 0.27 σg/in^2	< 27 σg/kg
Blank Paper	< 0.27 σg/in^2	< 27 σg/kg

Table 5. Migration of the FCS into 50% ethanol

[9]As discussed on page 6 of the FCN, the FCS in its acid form is not soluble in water and must be partially neutralized with ammonia in order to apply the product to paper.

[10]Migration into food is based on the assumption that 10 grams of food is in contact with 1 in^2 of paper.

Paper Sample	Migration from Paper	Migration into Food[10]
Wet End Addition (WEA), partially neutralized, 1.5 wt-% FCS	< 0.28 σg/in^2	< 28 σg/kg
WEA, completely neutralized, 1.5 wt-% FCS	< 0.27 σg/in^2	< 27 σg/kg
Blank Paper	< 0.6 σg/in^2	< 60 σg/kg

From the data in Table 4, it can be seen that no migration from the paper samples treated with the FCS at the wet end (WEA) or the size press (SPA) was found in 10% ethanol at a level corresponding to 0.27 σg/in^2, or 27 σg/kg into paper, which is the limit of detection for the analytical method (LOD= 10 σg/ml calculated as in Appendix IV Table 5, footnote b). Table 5 also shows that no migration from WEA paper treated with the FCS was found in 50% ethanol at 0.27 σg/in^2.[11] However, the notifier states that SPA paper treated with 1.5 wt-% of the FCS in 50% ethanol exhibited migration values of 50 σg/in^2.[12] The notifier believes that 50% ethanol is an aggressive solvent for paper, and the higher migration values are a result of this. As a result, the notifier also performed migration tests using n-heptane as a fatty food simulant. These results are presented below in Table 6 for the SPA samples as taken from Table 6 in Appendix IV of the FCN.

Table 6. Migration of the FCS into n-heptane

Paper Sample	Migration from Paper	Migration into Food[10]
Size Press Addition (SPA), partially neutralized, 1.5 wt-% FCS	< 0.22 σg/in^2	< 22 σg/kg
SPA, completely neutralized, 1.5 wt-% FCS	< 0.22 σg/in^2	< 22 σg/kg
Blank Paper	< 0.22 σg/in^2	< 22 σg/kg

As can be seen from Table 6, migration into n-heptane was below the LOD, which corresponds to 0.22 σg/in^2. The use of n-heptane, however, is not currently recommended in our Chemistry Guidance document for use as a fatty food simulant for paper. Thus, we will use the value of 50 σg/in^2, or 50#σg/kg into food, reported for 50% ethanol to model migration into fatty food.

Validation of the analytical method is discussed in section F of the FCN (p. 11) and Appendix IV. Analyses for 10% ethanol, 50% ethanol and n-heptane were validated by spiking all extracts at a level corresponding to 0.50 σg/in^2. Average percent recoveries varied from 92-116 percent (see Tables 8-10 of the TNO report in Appendix IV). Validation was repeated for 10% ethanol and n-heptane (contained in the September 21, 2001 TNO report addendum in Appendix IV) using a spiking level corresponding to 0.26 σg/in^2 with percent recoveries

[11]The notifier suggests (as discussed in Appendix IV, Table 5, footnote e) that the high migration value for the blank paper is the result of migration of polyethyleneglycol polymer containing phosphate end groups eluting at the same retention time as perfluoroether phosphates.

[12]The notifier has not provided actual data for the migration of the FCS from SPA paper into 50% ethanol. Due to the resulting low exposure values for the FCS, however, we have decided that it is not necessary to request the missing data.

ranging from 87 to 95%. The method provides acceptably reproducible results, and can be considered adequately validated.

Extraction of EO and 1,4-dioxane

Extraction experiments for EO and 1,4-dioxane are discussed in the TNO report contained in Appendix IV of the FCN. The notifier had difficulty analyzing the FCS for EO and 1,4-dioxane. Consequently, they chose to analyze the precursor to the FCS, EPFED, for these substances by means of head space GC-MS. In a headspace vial, a 1 gram sample of the FCS precursor was dissolved in 1 ml of dimethylacetamide (DMA) along with 50 σl of 1,3-butadiene internal standard. The vials were sealed and then heated in an agitator for 45 minutes at a temperature of 90∀C. The samples were analyzed in triplicate and quantified by means of the 1,3-butadiene internal standard and an external calibration curve developed from standard solutions of EO and 1,4-dioxane. EO and 1,4-dioxane were not found to be present in the FCS precursor at detection limits of 0.24 σg/g and 1.6 σg/g, respectively. Validation of the analytical technique showed a mean recovery of 98% for EO standard addition at a level of 0.9693 σg/g, and a mean recovery of 99% for standard addition of 1,4-dioxane at a level of 7.776 σg/g.

These analyses are adequate.

Analysis of ·9999

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Exposure

Oligomers of the FCS

Exposure to oligomers of the FCS is discussed in Section F of the FCN (pp. 10-13). The notifier determined an oligomers dietary concentration (DC) of 2.5 ppb. We have determined a slightly higher DC based on the following rationale. As discussed above, a value of 27 σg/kg is appropriate to model migration into aqueous, acidic, and low alcohol foods (from the 10% ethanol studies). However, we will use the reported value of 50 σg/kg to model migration into fatty foods (from the 50% ethanol studies), and not 22 σg/kg (from n-heptane) as used by the notifier . Using the food-type distribution factors (f_t) for the uncoated paper packaging category (f_{aq} = 0.57, f_{ac} = 0.01, f_{al} = 0.01, f_{fat} = 0.41), the weighted-average concentration of FCS oligomers in food (<M>) is:

$$\{ M \} | (f_{aq} 2 f_{alc} 2 f_{ac}) \Delta M_{10\% \text{ ethanol}} 2 f_{fatty} \Delta M_{50\% \text{ ethanol}}$$

$$| (0.57 2 0.01 2 0.01) \Delta \frac{27\,\mu g}{kg} 2 0.41 \Delta \frac{50\,\mu g}{kg}$$

$$| 36.4\,\mu g/kg$$

Using a consumption factor (CF) of 0.1 for uncoated and clay coated paper, the revised DC is:

DC = CF x M = 0.1 x 36.4 σg/kg
= 3.6 σg/kg or 3.6 ppb

Assuming a daily diet of 3000 grams of food/p/d, the estimated daily intake (EDI) of the FCS oligomers is 11 σg/p/d.

Impurities

Ethoxylated Perfluoroether diol (EPFED)

In the original submission, the notifier stated that the LC-MS method used for detection of oligomers of the FCS would also detect residual EPFED. Based on this assumption, the notifier stated that the DC for this impurity would be < 2.5 ppb (the value stated by the notifier for oligomers of the FCS). We requested data from the notifier showing that EPFED was in fact detected along with the FCS in their migration testing protocol. In their 12/19/01 submission, the notifier stated that while they still believed that EPFED would have a retention time similar to that of oligomers of the FCS, they did not have conclusive data showing retention time overlap, or that the response factors would be similar. In light of this, they presented an exposure estimate based on 100% migration of EPFED and the following assumptions:
1.) The FCS is present in paper at a maximum level of 1.5 wt-%.
2.) A gel permeation chromatograph of EPFED (see Appendix II) showed that less than 3.8% of the species analyzed had a molecular weight below 1000 daltons.[13]
3.) A paper basis weight of 50 mg/in^2.
4.) Assumption of 10 grams of food in contact with 1 in^2 of paper.
5.) Data showing that on average the FCS contains EPFED at a level of 0.67%.
6.) CF of 0.1 for uncoated and clay coated paper.

Thus, the EDI for EPFED can be calculated as follows:

$$DC_{EPFED} | \frac{0.015\,g\,FCS}{1\,g\,paper} \Delta \frac{0.0067\,g\,EPFED}{g\,FCS} \Delta 0.038 \Delta \frac{0.050\,g\,paper}{in^2} \Delta \frac{in^2}{10\,g\,food} \Delta 0.1$$

$$| 1.9\,\mu g/kg \quad or\,1.9\,ppb$$

[13]The 12/19/01 submission stated 2%, however analysis of their table showed that the value was approximately 3.8% rather than 2%.

Assuming a diet of 3000 g food/p/d, this results in an EDI of 5.7 σg/p/d for EPFED. We believe that this estimate is conservative.

Isobutyl Alcohol (IBA)

IBA was reported to be present in the FCS at a maximum level of 0.3%. Assuming 100% migration, and using the same assumptions listed above for EPFED (except for assumption 2 and 5), the DC and EDI for IBA are calculated to be 23 σg/kg (23 ppb) and 69 σg/p/d, respectively. We believe that these estimates are conservative.

EO and 1,4-dioxane

EO and 1,4-dioxane were not found in the EPFED precursor to the FCS at detection limits of 0.24 mg/kg and 1.6 mg/kg, respectively. The dietary concentration for EO can be calculated as:

$$DC_{EO} = \frac{0.24 \times 10^{-6}\ \text{g EO}}{\text{g FCS}} \times \frac{0.015\ \text{g FCS}}{1\ \text{g paper}} \times \frac{0.050\ \text{g paper}}{\text{in}^2} \times \frac{\text{in}^2}{10\ \text{g food}} \times 0.1$$

$$= 1.8\ \text{ng/kg or } 1.8\ \text{pptr EO}$$

This would correspond to an EDI of 5.4 ng/p/d for EO. We can use the same assumptions (and based on an upper limit concentration of 1.6 mg/kg) to calculate a DC and an EDI for 1,4-dioxane of 12 ng/kg (or 12 pptr) and 36 ng/p/d, respectively.

Table 7. Summary of exposure estimates

Compound	CAS Reg. No.	DC (σg/kg (ppb))	EDI[14] (σg/p/d)
Oligomers of the FCS	200013-65-6	3.6	11
EPFED	162492-15-1	1.9	5.7
999	9999999	999	999
9999	99999999	99999999999	99999999999999999
EO	75-21-8	0.0018	0.0054
1,4 dioxane	123-91-1	0.012	0.036

Risk Assessment for Ethylene Oxide and 1,4 Dioxane

Previously, the Quantitative Risk Assessment Committee (QRAC) determined a carcinogenic unit risk of 1.12×10^{-1} (mg/kg bw/d)$^{-1}$ for EO, and 2.1×10^{-3} (mg/kg bw/d)$^{-1}$ for 1,4-dioxane (see QRAC report dated 7-1-93). The EDIs for EO and DX are 5.4 ng/p/d (5.4×10^{-6} mg/p/d) and 36 ng/p/d (36×10^{-6} mg/p/d), respectively for the uses presented in this FCN. For a 60 kg person, the EDI for EO becomes:

$EDI_{EO\ 60\ kg\ person} = [(5.4 \times 10^{-6}\ mg/p/d)/(60\ kg\text{-}bw/p)] = 9 \times 10^{-8}$ mg/kg-bw/d

Multiplying the above calculated EDI for EO by the unit risk for EO yields an upper-bound risk of :

Upper bound risk$_{EO}$ = $\{(9 \times 10^{-8}$ mg/kg-bw/d) x $[1.12 \times 10^{-1}$ (mg/kg-bw/d)$^{-1}]\}$
$= 1 \times 10^{-8}$

Similarly, for 1,4-dioxane (DX) the EDI for a 60 kg person would be:

$EDI_{DX\ 60\ kg\ person} = [(36 \times 10^{-6}\ mg/p/d)/(60\ kg\text{-}bw/p)] = 6 \times 10^{-7}$ mg/kg-bw/d

Multiplying the above calculated EDI for DX by the unit risk for DX yields an upper-bound risk of :

Upper bound risk$_{DX}$ = $\{(6 \times 10^{-7}$ mg/kg-bw/d) x $[2.1 \times 10^{-3}$ (mg/kg-bw/d)$^{-1}]\}$
$= 1.3 \times 10^{-9}$

Notification Language

The language used in the 1/25/2002 acknowledgement letter is adequate.

Summary

[14]The EDI is based upon the assumption that a person consumes 3 kg of food per day.

The migration studies and exposure calculations for oligomers of the FCS led to the determination of a dietary concentration of **3.6 σg/kg** (or 3.6 ppb) which corresponds to an EDI of **11 σg/p/d**. Exposures were also determined and listed in Table 7 for impurities associated with the FCS. Risk assessments for ethylene oxide and 1,4-dioxane resulted in the calculation of upper bound unit risks of 1×10^{-8} and 1.3×10^{-9}, respectively.

We have no further questions

Daniel E. Folmer, Ph.D.

HFS-245 (Begley); 246 (Kuznesof, R/F)
HFS-246:DFolmer:208-3148:FCN195 Phase II Chemistry Memo
Init:SCarberry:1/22/2002
Init:ABailey: 2/11/2002
Final: def: 2/11/2002

SOLVAY SPECIALTY FCN 398

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

The FCS is the ammonium salt of the polymer with the CAS name "ethene, tetrafluoro-, oxidized, polymerized, reduced."

2. CAS Registry Number

No CAS Registry No. has been assigned to the FCS. The CAS Registry No. for the acidic form of the polymer is "69991-62-4."

3. Trade or Common Name

4. Other Chemical Names (IUPAC, etc.)

Perfluoropolyether dicarboxylic acid ammonium salt

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is the ammonium salt of perfluoropolyether dicarboxylic acid, specifically, resulting from the neutralization of perfluoropolyether dicarboxylic acid (CAS Registry Number 69991-62-4) with aqueous ammonia (CAS Registry Number 1336-21-6). The structure of the polymer may be represented as follows:

$$H_4N^{+}\text{-}OOC\text{-}CF_2\text{-}(OCF_2\text{-}CF_2)_n\text{-}(OCF_2)_m\text{-}O\text{-}CF_2\text{-}COO^{-}NH_4^{+}$$

The minimum M_w and M_n specifications for the polymer are 2000 and 1300 Dalton, respectively.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Typical Infra-red, and ^{19}F-NMR spectra of the FCS may be found in Appendix I.

000007

Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
Perfluoropolyether dicarboxylic acid	69991-62-4	Polymer
Ammonium hydroxide	1336-21-6	Provide counter ion for acid moieties on the polymer
		Solvent
		Solvent
		Solvent
		Solvent
		Solvent

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

Fluorolink PT 5071 is the ammonium salt of perfluorpolyether dicarboxylic acid. The acid form of perfluoropolyether dicarboxylic acid is insoluble in water, thus it is necessary to neutralize the acid groups with ammonium hydroxide to solubilize the product for use in the wet-end of the paper making process. The ammonium hydroxide partially salifies the terminal carboxylate moieties of the polymer forming a stable aqueous dispersion. Perfluoropolyether dicarboxylic acid has been assigned the CAS Registry Number 6991-62-4; a CAS registry number has not been assigned to the corresponding ammonium salt of this polymer. The material data safety sheets (MSDS) for tetrafluorethylene, ammonium hydroxide, perfluorpolyether dicarboxylic acid, and the ammonium salt of perfluorpolyether dicarboxylic acid are attached in Appendix II. The confidential details of the manufacturing process for perfluoropolyether dicarboxylic acid and the details concerning the formation of the ammonium salt are attached in Confidential Appendix III. The organic solvents indicated above are potential alternatives to each other; only one of the solvents will be used in a given formulation at a maximum use level of [redacted] the balance of the formulation being water.

000008

Section B - MANUFACTURE - Continued

List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual	Maximum Residual
Fluoride	n/a	< 30 ppm	30 ppm (See Appendix IV)
Tetrafluoroethylene	116-14-3	< 10 ppb	10 ppb (See Appendix IV)

Ensure that exposures to these substances are addressed in Section II.G of this form.

000009

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches (See Appendix III)

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

Property	Max. Value	Min. Value	Individual Batch Values
M_w	4000	2000	3125, 2793, 3387 Dalton (See Appendix V)
M_n	2000	1300	1710, 1518, 1334 Dalton (See Appendix V)
Appearance		Clear	Clear, clear, clear (See Appendix V)
pH			
Solids			

000010

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Approximately 22% of the polymer is oligomeric, with a molecular weight less than 1000 Daltons. Molecular weight was determined by gel permeation chromatography (GPC) on the methyl ester derivative of the polymer for ease of analysis. See Appendix V for GPC data. [redacted] is the tradename for the tetrafluoropolyether dicaboxylic acid polymer).

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil and water repellant in paper and paperboard, and is added prior to the sheet forming process. The maximum addition rate is [redacted] of polymer by weight of dry finished paper and paperboard. The FCS is fully substantive to the fiber and remains in the finished paper.

Suggested language for describing the FCS and the applicable limitations for its use in contact with food is proposed in Appendix XIV.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Perfluoropolyether dicarboxylic acid, ammonium salt used as an oil and/or water repellant in paper and paperboard	All	B through H

000011

Section D - INTENDED USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

000012

State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil and water repellant properties are measured by the Kit Test (TAPPI Method 559), and the $Cobb_{60}$ Test (TAPPI Method 441) respectively Copies of these methods are attached in Appendix VI. The Kit Value represents the repellency and/or antiwicking characteristics to oil of paper and paperboard treated with fluorochemicals. The Cobb value indicates the mass of water absorbed by one square meter of paper over a specific time. Typical values for Fluorolink PT 5071 treated paper:

Dry weight % PT 5071	Kit Value ($g/m^2/d$)	$Cobb_{60}$ value (g/m^2)
0.4	7	50
0.6	8	40
0.8	10	35
1.0	10	30

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

000013

Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

000014

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Test specimens, in the form of 10 cm by 15 cm paper sheets with a basis weight of 52 mg/in^2, were prepared with 1% (w/w) FCS added to the pulp slurry. Similar control specimens were prepared without the addition of the FCS. Both test and control specimens were sectioned into 1 cm by 3 cm pieces, and 50 of these 3 cm^2 (0.03 dm^2) sections were added to headspace vials (1.5 dm^2 total surface area) containing 40 mL of pre-heated food simulating solvent. The headspace vials were sealed and the resulting volume to surface area was 27 mL/dm^2 (2 mL/in^2). The specimens were immersed in food simulating solvent, however, the surface area of a single side was used in calculating the volume to surface area ratio due to the fact that the specimen thickness was less than 254 µm (0.01 in). The resulting extracts were clear in appearance and no precipitate was observed.

A full report of the migration study is provided in Appendix VII.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Water, iso-octane, and a 3% aqueous solution of acetic acid were used as food simulating solvents. Prior consent for use of iso-octane as a fatty food simulant was obtained from FDA/CFSAN (tracking number CTS 84710, see Appendix VIII). Water, rather than 10% ethanol was selected as the simulant for aqueous foods for reasons analogous to the justification presented in the aforementioned correspondence for use of iso-octane as the fatty simulant. Specifically, the FCS is so soluble in alcohol, that the use of alcohol unreasonably exaggerates the potential migration of the FCS to aqueous and fatty foods. Because alcohol was not used as a simulant in the migration testing, and because we intend to use this FCS with all food types, we have conducted 100% migration calculations for use in the EDI determination for the exposure contribution of the FCS oligomers from alcoholic foods.

Test and control specimens were extracted in triplicate in all three food simulating solvents for 2 hr at 100°C, followed by an additional 238 hours at 40°C (Condition of Use B). It may be noted upon review of the migration testing report that in addition to extraction under FDA conditions, separate extractions in iso-octane and aqueous acetic acid were conducted for 4 hours at 60°C and 100°C, respectively, for the purpose of submitting a dossier to permit the use of the FCS for food-contact applications in the European Union. These data were not relied upon for the purposes of this submission as migration data collected according to FDA's Chemistry Guidelines is available.

000015

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

000016

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Paper containing 1%		Water	100°C for 2 hr	0.0019 mg/in^2 0.0012 mg/in^2 0.0012 mg/in^2	0.0017 mg/in^2
Paper containing 1%		Water	100°C for 2 hr, followed by 238 hr at 40°C	0.0013 mg/in^2 0.0015 mg/in^2 0.0006 mg/in^2	0.0011 mg/in^2
Paper containing 1%		3% acetic acid	100°C for 2 hr	<0.0002 mg/in^2 <0.0002 mg/in^2 <0.0002 mg/in^2	<0.0002 mg/in^2
Paper containing 1%		3% acetic acid	100°C for 2 hr, followed by 238 hr at 40°C	<0.0002 mg/in^2 <0.0002 mg/in^2 <0.0002 mg/in^2	<0.0002 mg/in^2
Paper containing 1%		Iso-octane	100°C for 2 hr	<0.0002 mg/in^2 <0.0002 mg/in^2 <0.0002 mg/in^2	<0.0002 mg/in^2
Paper containing 1%		Iso-octane	100°C for 2 hr, followed by 238 hr at 40°C	<0.0002 mg/in^2 <0.0002 mg/in^2 <0.0002 mg/in^2	<0.0002 mg/in^2

The water extract was directly analyzed. The following calculation demonstrates conversion of aqueous concentration to migration in mg/in^2:

(1.1 µg/mL water) x (40 mL water/1.5 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0019 mg/in^2 paper.

Prior to analysis of the acetic acid and iso-octane extracts, 40 mL of extract was evaporated, and the residue taken up in 10 mL of iso-propanol (IPA), or water respectively. Concentrations are reported as µg/mL oligomer in IPA or water. The following is an example of how these values were used to calculate the corresponding migration levels in mg/in^2:

(0.48 µg/mL IPA) x (40 mL acetic acid/1.5 dm^2 specimen) x (10 mL IPA/40 mL acetic acid) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0002 mg/in^2 paper.

000017

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Extract Identification	Replicate	Fortification Level (µg/mL)[a]	Amount Detected (µg/mL)	Recovery	Mean Recovery (%)
240 hr. iso-octane extracts of FCS treated paper	1	0.122	0.107	Detected	Detected
	2	0.122	0.098	Detected	
	3	0.122	0.091	Detected	
240 hr. acetic acid extracts of FCS treated paper	1	0.123	0.098	Detected	Detected
	2	0.123	0.097	Detected	
	3	0.123	0.095	Detected	

a. Level 1 Fortification: (0.122 µg Fluorolink PT 5071/mL simulant) x (40 mL simulant/1.5 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0002 mg Fluorolink PT 5071/in^2 paper.

Extract Identification	Replicate	Initial Concentration (µg/mL)	Amount Added (µg/mL)	Amount Detected (µg/mL)	Amount Recovered (µg/mL)	Recovery (%)	Mean Recovery (%)
240 hr water extracts of FCS treated paper	1	0.74	0.268[b]	1.012	0.274	102	99±2
	2	0.88	0.268	1.140	0.260	97	
	3	0.36	0.268	0.623	0.263	98	
	1	0.74	0.537[c]	1.253	0.515	96	101±6
	2	0.88	0.537	1.412	0.532	99	
	3	0.36	0.537	0.940	0.580	108	
	1	0.74	1.074[d]	1.833	1.095	102	100±5
	2	0.88	1.074	1.986	1.160	103	
	3	0.36	1.074	1.370	1.010	94	

b. Level 2 Fortification: (0.268 µg [redacted] mL simulant) x (40 mL simulant/1.5 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0005 mg [redacted] /in^2 paper.

c. Level 3 Fortification: (0.537 µg [redacted] mL simulant) x (40 mL simulant/1.5 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.001 mg [redacted] /in^2 paper.

d. Level 4 Fortification: (1.074 µg [redacted] mL simulant) x (40 mL simulant/1.5 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.002 mg [redacted] /in^2 paper.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

Substance	100% Migration (ppb)
Fluoride	7.5
TFE	0.0025
Oligomers	11,000 (migration to alcoholic foods)

Please see Appendix IX for complete details

Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Substance	Dietary exposure (ppb)
Oligomers	22.7
Fluoride	0.75
TFE	0.00025

Please see Appendix IX for complete details.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

000019

Memorandum

AD

Date: March 23, 2004

From: Division of Food Contact Notifications
Chemistry Group I, HFS-275

Subject: FCN 398: Solvay-Solexis S.p.A., through Keller & Heckman; submissions of 12/11/03 and 1/26/04. Perfluoropolyether dicarboxylic acid, ammonium salt, as a grease-proofing agent for paper/paperboard.

To: Division of Food Contact Notifications
Regulatory Group II, HFS-275
Attn: P. Honigfort, Ph.D.

Keller & Heckman (K&H), on behalf of Solvay-Solexis, has submitted a food contact notification (FCN) to allow perfluoropolyether dicarboxylic acid, ammonium salt (trade name Fluorolink PT 5071) to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard intended to contact all types of food under conditions of use B through H. The food-contact substance (FCS) will be added prior to the sheet-forming process. The FCS is not currently authorized for any uses in or on food.

IDENTITY, MANUFACTURE, AND COMPOSITION

A. Identity

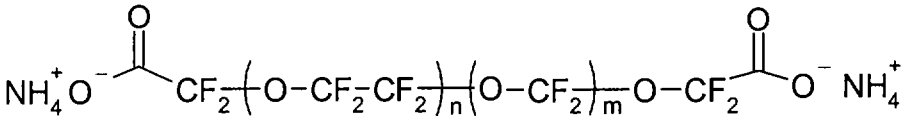
Chemical Name and CAS Registry No.

ammonium salt of ethene, tetrafluoro-, oxidized, polymerized, reduced

CAS Reg. No. for the acid form of the FCS: 69991-62-4

Common Names perfluoropolyether dicarboxylic acid ammonium salt

Structure



Molecular Weight

M_w 2000-4000 Daltons (3100 avg. for 3 production batches)
M_n 1300-2000 Daltons (1520 avg. for 3 production batches)
22 wt-% is comprised of oligomers of MW < 1000
(See Part II.C.2 of Form 3480 and Appendix 5, pp. 64-71 of the FCN for supporting gel permeation chromatography (GPC) data.)

Physical Properties/Specifications

Appearance	Clear liquid
pH	7.5 – 9
% Solids	19.5 – 21.5
Density	1.0 – 1.1 g/cm^3
Water Solubility	Miscible

See Part II.C.2.a of Form 3480; Appendix 2, p. 21; and Appendix 5, pp. 72-79 for supporting data.

Data to Characterize the FCS

IR and ^{19}F NMR spectra of three production batches of the FCS are provided in Appendix 1 of the FCN.

The FCS is adequately identified.

B. Manufacture (Part II.B.2 of Form 3480 and Appendix 3 to the FCN)

Perfluoropolyether dicarboxylic acid ([redacted], the acid form of the FCS, is manufactured [redacted]

Because [redacted] is insoluble in water, it is ammoniated in order to allow it to solubilize for use in the wet end of the papermaking process. The FCS is dissolved in water and one of the following organic solvents, [redacted]

[redacted] is prior-sanctioned for the notifier's intended use in 21 CFR 181.30 (Substances used in the manufacture of paper and paperboard products used in food packaging). [redacted] is affirmed as generally recognized as safe (GRAS) in [redacted]

Neither [redacted] is specifically authorized for the notifier's intended use. However, these substances are regulated without limitation in §176.200 (Defoaming agents used in coatings) and §176.210 (Defoaming agents used in the manufacture of paper and paperboard). It is our judgment that the very low exposures resulting from the proposed use of these alcohols (they are highly water-soluble and volatile and would be almost entirely lost in the whitewater or during the drying stage of paper manufacture) would be subsumed by those evaluated in support of the regulated uses in §176.200 and §176.210.

K&H has adequately described the manufacture of the FCS.

Potential for PFOA Formation

It is our judgment that perfluorooctanoic acid (PFOA) will not be present in the subject FCS. PFOA is not used as a starting material in the manufacture. The oxidative polymerization used to produce the [redacted] precursor of the FCS is such that only $-CF_2O-$ and $-CF_2CF_2O-$ units form, i.e., the maximum length of any perfluoro group in the polymer is C_2. According to the notifier, "The reactivity of the fluorinated radicals towards oxygen is so high that no oligomers of TFE can be detected" (see Appendix 3, p. 27 of the FCN). We agree with the notifier that the likelihood of the formation of C_3 or greater perfluoro groups (C_8 is required to form PFOA) is essentially zero.

C. Composition

Two potential impurities, TFE and F^-, and their typical residual levels in the finished [redacted] (suspension containing 20 wt-% FCS solids) are listed in Part II.B.3 of Form 3480. For TFE, adequate analytical data were provided (Appendix 4, pp. 32-45) to support the < 10 µg/kg residual level determined in three production batches of the Fluorolink suspension by headspace gas chromatography with flame ionization detection. TFE was not detected in any of the samples. For F^-, however, K&H provided only a description of the ion chromatography method used (see Appendix 4, pp. 59-63) to support their claim that the F^- levels in the [redacted] suspension are < 30 mg/kg. In response to our 1/21/04 deficiency letter, K&H provided highly detailed raw data, chromatograms, calculations, and validation data in their 1/26/04 submission to demonstrate that the F^- levels in three production batches of the [redacted] suspension were < 30 mg/kg, the limit of quantification (LOQ) of the method. Fluoride ion was detected in each of the samples, but the levels were below the LOQ (see chromatograms 42, 43, and 44 at the end of the 1/26/04 submission).

Adequate GPC data for three production batches of the FCS (i.e., the solids portion of the [redacted] suspension) were provided in Appendix 5 to demonstrate that the concentration of oligomers of MW < 1000 Daltons is 22 wt-%. This value was used to calculate exposure to the FCS from use in contact with alcoholic foods (see below).

Based on the fact that the free acid precursor [redacted] is neutralized with ammonium hydroxide, a reaction that goes to 100% completion, exposure to [redacted] will be essentially zero. Since [redacted] is not soluble in water, any that might be present in the

FCS would not go into solution during papermaking and would therefore not be retained on the paper.

Based on the manufacturing information provided in Appendix 3 (see especially p. 31), we do not expect any additional impurities to be present in the subject FCS.

The impurities are adequately described.

D. Stability

The FCS is not expected to degrade under the intended conditions of use (see Part II.E of Form 3480).

INTENDED USE AND USE LEVEL

The subject FCN proposes to allow [redacted] to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard in paper and paperboard intended to contact all types of food under conditions of use B through H. The FCS will be added prior to the sheet-forming process. The FCS is fully substantive to the fiber and will remain in the finished paper.

TECHNICAL EFFECT

Adequate technical effect data to support use of the FCS as an oil and water repellent are provided in Part II.D.3 of Form 3480 and in Appendix 6. The standard TAPPI (Technical Association of the Pulp and Paper Industry) "Kit" and "Cobb" tests were used to demonstrate increasing grease resistance and decreasing water absorptiveness, respectively, with increasing concentrations of the FCS in paper.

MIGRATION DATA FOR TOTAL OLIGOMERS (Appendix 7, summary in Part II.F.1 of Form 3480)

Migration tests on paper treated with [redacted] were conducted by TNO Nutrition and Food Research, Netherlands, into water, 3% acetic acid, and isooctane to simulate condition of use B (100° C for 2 hr followed by 40° C for 10 d). TNO stated that the high solubility of the FCS in aqueous ethanol mixtures would yield exaggerated migration results, hence TNO's use of water, 3% acetic acid, and isooctane as food simulants. We have accepted isooctane as a fatty-food simulant on several occasions in the past and specifically allowed its use for the subject FCN (see Appendix 8 of the FCN and CTS 84710, memorandum dated 7/10/03, R. Costantino to P. Honigfort).

Total oligomers were determined in these studies via liquid chromatography with mass spectrometric detection (LC/MS). The retention time of the single analyte peak for the FCS

varied within the range 1.4 to 2.6 min, depending on the food simulant. The entire mass range of m/z 120-2000 was used to quantify the total oligomers comprising the analyte peak. TNO has provided adequate sample and validation data, chromatograms, calibration curves, and calculations to support the migration measurements reported. Although raw peak areas were not provided for the water samples, we believe that the high level of detail in the description of the analytical method and in the other data support TNO's results for the water samples. The migration test results are summarized in Table 1.

Table 1. Migration Values for Perfluoropolyether Oligomers from the FCS

Food Simulant	Test Conditions Yielding Maximum Migration	Conc. in Analyzed Migration Sample (mg/L)[a]	Migration Value (mg/in^2)	Conc. in Food (mg/kg)[b]
Water	2 hr at 100° C	0.83	0.0014[c]	0.14
3% Acetic Acid	2 hr at 100° C followed by 10 d at 40° C	< 0.48[d]	< 0.0002	< 0.02
Isooctane	"	< 0.51[d]	< 0.0002	< 0.02

[a]Average value for three replicate samples.
[b]Assuming 10 g of food contact 1 in^2 of packaging material.
[c]K&H erred in calculating 0.0017 mg/in^2 as the average of 0.0019, 0.0012, and 0.0012 mg/in^2.
[d]Oligomers were not detected under any testing conditions.

For the migration studies, paper samples of basis weight 0.052 g/in^2 were prepared by the addition of 1 wt-% of the FCS, based on the weight of the dry finished paper, to the pulp slurry. Each sample, consisting of a one-sided surface area of 23.2 in^2 (1.5 dm^2), was cut into small pieces and placed in a crimp-top vial with 40 mL of preheated food simulant for a volume-to-surface area ratio of 1.7 mL simulant/in^2. Although this value is significantly lower than our recommended 10 mL simulant/in^2, the facts that 1) the migration samples were "clear in appearance and no precipitate was observed" (see Part II.F.1.a of Form 3480), and 2) that the spike-and-recovery validation experiments resulted in recoveries of 72 to 101% of the FCS spiked into the migration samples, demonstrate that the migration samples did not become saturated with the oligomers.

The water samples were analyzed directly, while the 3% acetic acid and isooctane samples were evaporated to dryness and redissolved into 10 mL isopropanol and water, respectively, prior to analysis. An example calculation of the migration value (mg/in^2) for the oligomers in water follows:

$$\frac{0.83 \times 10^{-6} \text{ g oligomer}}{\text{g water}} \Big| \frac{40 \text{ g water}}{23.2 \text{ in}^2 \text{ paper}} = 0.0014 \text{ mg/in}^2$$

For the other simulants, the result was divided by a factor of 4 (40 mL/10 mL) to account for the preconcentration step.

The limits of detection (LOD) of the LC/MS method were 0.48 mg/L for 3% acetic acid, 0.51 mg/L for isooctane, and 0.22 mg/L for water. The LODs for acetic acid and isooctane were based on the lowest standard concentration used to construct the calibration curve. The LOD for water was based on the "Within Laboratory Detection Limit," which was twice as high as the lowest standard concentration used to construct the calibration curve. TNO apparently used this higher LOD to account for the variability of the water measurements.

EXPOSURE ESTIMATES

A. 100% Migration Calculations (Appendix 9, summary in Part II.F.2 of Form 3480)

Oligomers into Alcoholic Food Simulant

Since an alcoholic food simulant was not used in the migration tests, K&H assumed 100% migration of the oligomers of MW < 1000 determined by GPC (22 wt-% of the FCS) for the contribution of alcoholic foods to the total exposure to the oligomers. The calculation, which is based on a maximum concentration of 1 wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material, follows:

$$\frac{0.22 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.01 \text{ g FCS}}{\text{g paper}} \right| \frac{0.05 \text{ g paper}}{\text{in}^2} \left| \frac{\text{in}^2}{10 \text{ g food}} \right. = 11 \text{ mg/kg oligomers in food}$$

Residual Impurities

K&H used the residual levels of TFE and F$^-$ given in the "Composition" section above to correctly calculate 100% migration values for these impurities (see Appendix 9). The following is an example calculation for TFE, using the typical 20 wt-% solids value given in the "Physical Properties/Specifications" section above for the concentration of the FCS in the Fluorolink suspension, a maximum concentration of 1 wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material:

$$\frac{10 \text{ ng TFE}}{\text{g [redacted]}} \left| \frac{1 \text{ g [redacted]}}{0.20 \text{ g FCS}} \right| \frac{0.01 \text{ g FCS}}{\text{g paper}} \left| \frac{0.05 \text{ g paper}}{\text{in}^2} \right| \frac{\text{in}^2}{10 \text{ g food}} = 2.5 \text{ ng/kg TFE in food}$$

The results of all the 100% migration calculations are shown in Table 2.

Table 2. Concentrations of FCS Components in Food, Assuming 100% Migration

Component	Conc. in Food
Oligomers (for alcoholic food contribution only)	11 mg/kg
TFE	2.5 ng/kg
F^-	7.5 µg/kg

B. Exposure Calculation (Appendix 9, summary in Part II.G.1 of Form 3480)

K&H has correctly calculated the exposures to the components of the subject [redacted] based on the migration data provided by TNO for oligomers in aqueous, acidic, and fatty foods, and assuming 100% migration of the oligomers into alcoholic foods and of TFE and F^- into all foods. We note, however, that we have traditionally used a consumption factor (CF) of 0.05 for paper/paperboard treated with grease-proofing agents, rather than the CF of 0.1 that K&H used for uncoated paper.[1] We will use the CF of 0.05, the food-type distribution factors (f_T) given in our "Recommendations" for uncoated paper, and the migration values given in Tables 1 and 2 to calculate the dietary concentration (DC) and estimated daily intake (EDI) of the oligomers:

$$DC = 0.05\ CF\ [(0.57\ f_{aq})(0.14\ mg/kg) + (0.01\ f_{ac})(0.02\ mg/kg) + (0.01\ f_{al})(11\ mg/kg) + + (0.41\ f_{fa})(0.02\ mg/kg)] = 9.9\ ppb$$

$$EDI = (9.9 \times 10^{-9}\ g\ oligomers/g\ food)(3000\ g\ food/p/d) = 30\ \mu g/p/d$$

An example exposure calculation for TFE, using the 100% migration value given in Table 2, follows:

$$DC = (0.05\ CF)(\Sigma f_T = 1)(2.5\ ng/kg) = 0.00012\ ppb$$
$$EDI = (1.2 \times 10^{-13}\ g\ TFE/g\ food)(3000\ g\ food/p/d) = 0.36\ ng/p/d$$

The exposures to the components of [redacted] are summarized in Table 3.

Table 3. Exposures to Components of Fluorolink PT 5071

Substance	CAS Reg. No.	Function	DC (ppb)	EDI
Total oligomers		FCS itself	9.9	30 µg/p/d
TFE	116-14-3	Monomer	< 0.00012[a]	< 0.36 ng/p/d
Fluoride ion	16984-48-8	Impurity	< 0.38[b]	< 1.1 µg/p/d

[a]Below the LOD.
[b]Detected but below the LOQ.

[1] See, for example, FCN 59, memorandum dated 8/1/00, R. Costantino to E. Machuga.

C. Cumulative Exposures

The only component of [redacted] with a potential cumulative exposure issue is F^-. The U.S. Environmental Protection Agency (EPA) has established an enforceable drinking water standard for F^- of 4 mg/L.[2] However, EPA has also set a secondary F^- standard of 2 mg/L to protect against dental fluorosis. If we assume that all the liquid food in the daily diet has an F^- concentration of 2 mg/L (or 2 mg/kg) and that the daily diet consists of 1.5 kg of liquid food, we can calculate the EDI of F^- from fluoridated water as follows:

EDI = (2 mg F^-/kg liquid food)(1.5 kg liquid food/p/d) = 3 mg/p/d F^-

The EDI for F^- determined for the subject FCS is a factor of 3000 less than that determined for F^- from fluoridated drinking water. It is our judgment that use of the subject FCS will not increase the cumulative exposure to F^- from the daily diet.

ACKNOWLEDGMENT LETTER

The acknowledgment letter dated 2/13/04 is acceptable as written.

CONCLUSIONS

The exposures to the components of [redacted] from its use as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard in paper and paperboard intended to contact all types of food under conditions of use B through H are summarized in Table 3 above. The cumulative exposure to fluoride ion will not increase from use of this FCS. It is our judgment that PFOA will not be present in the subject FCS.

We have no questions.

/s/ [redacted]

Kristina E. Paquette, Ph.D.

[redacted]

[2] See http://www.epa.gov/safewater/mcl.html.

SOLVAY SPECIALTY 416

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene

2. CAS Registry Number

200013-65-6

3. Trade or Common Name

Fluorolink® F10, Fluorolink® PT5045

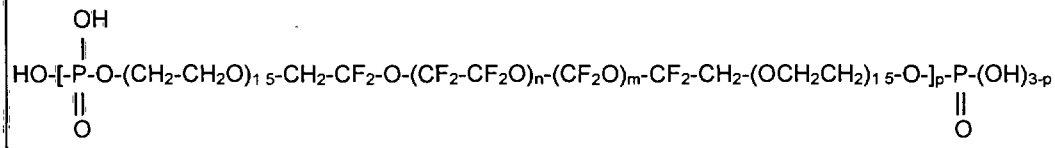
4. Other Chemical Names (IUPAC, etc.)

Phosphate ester of ethoxylated perfluoroether diol

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is the same material as is the subject of FCN 195, a description is presented again below for FDA's reference.



where p=1 for the monoester, p=2 for the diester, and n and m are approximately 6

The M_w and M_n for the polymer are typically 2200 and 1800, respectively.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

A characteristic IR spectrum of the FCS may be found in FCN 195, Appendix II.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
Ethoxylated perfluoroether diol	Not assigned	Polymer
Water	7732-18-5	Solvent
Phosphorous pentoxide	1314-56-3	Esterification reagent
Ethyl acetate	141-78-6	Solvent
Isobutyl alcohol	78-83-1	Solvent

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See FCN 195, Appendix I

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Section B - MANUFACTURE - Continued

List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
Isobutyl alcohol	78-83-1	<0.3%	0.3%
Tetrafluoroethylene	116-14-3	<28 ppb	28 ppb (LOD)
Ethylene oxide	75-21-8	<0.24 ppm	0.24 ppm (LOD)
1,4-Dioxane	123-91-1	<1.6 ppm	1.6 ppm
Ethoxylated perfluoroether diol	Not assigned	<5%	5%
Phosphoric acid	7664-38-2	<1%	1%
Ethanol	64-17-5	<0.1%	0.1%
Acetic acid	64-19-7	<0.2%	0.2%

Ensure that exposures to these substances are addressed in Section II.G of this form.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

Property	Max. Value	Min. Value	Individual Batch Values
Color	N/A	N/A	Pale brown
Appearance	N/A	N/A	Viscous liquid
Specific gravity (20°C)	1.73 g/cm^3		
Dynamic viscosity (20°C)	60,000 CPS		
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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

GPC data for the perfluoroether diol may be found in Appendix II of FCN 195. The molecular weight distribution of the phosphate ester is expected to be similar, although shifted slightly higher because of the diester formation.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

Flourolink® F10 is intended for use at a level of up to 1.5% by weight as an oil and water repellant in paper and paperboard in contact with all types of food under Conditions of Use B through H, as set forth in 21 C.F.R § 176.170(c), Table 2. It is also intended for use at a level of up to 1.0% by weight as an oil and water repellant in paper and paperboard in contact with all types of food in microwave susceptor applications. Flourolink® F10 is added prior to sheet formation, or at the size press by weight of dry finished paper or paperboard. Suggested language for describing the FCS, and the applicable limitations for its use in contact with food are given in Appendix V to this submission.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

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Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
Flourolink® F10 at a level not to exceed 1.5 weight percent in dry finished paper or paperboard as an oil and water repellant	All	B through H
Flourolink® F10 at a level not to exceed 1.0 weight percent in dry finished paper or paperboard as an oil and water repellant	All	Microwave susceptor

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

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State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

F10 imparts oil and water resistance to paper and paperboard. Data demonstrating the oil and water repellence properties of the FCS were included in FCN 195, Section E. The TAPPI Test Methods are presented in Solvay Solexis' FCN 398, Appendix 6, and are incorporated herein by reference.

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

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2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No.	Structure

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Full migration testing reports are included as Appendices I and II (supporting Condition of Use B, and microwave applications, respectively).

For the Condition of Use B application, test specimens, in the form of 10 cm by 15 cm paper sheets with a basis weight of 52 mg/in^2 were prepared with 1.5% (w/w) FCS added to the pulp slurry. A similar set of test specimens, differing only in that the FCS was added at the size press, were also prepared. Both types of test specimens were sectioned into 1 cm by 3 cm pieces, and 50 of these 3 cm^2 (0.03 dm^2) portions were added to a headspace vial (1.5 dm^2 total surface area) containing 40 mL of preheated food simulating solvent. Triplicate headspace vials were prepared for each specimen/type of extraction condition. The headspace vials were sealed, and the resulting volume to surface area was 27 mL/dm^2 (2 mL/in^2). The specimens were immersed in food simulating solvent, however, the surface area of a single side was used in calculating the volume-to-surface area ratio as the specimen thickness was less than 254 µm (0.01 in).

For the microwave application, test specimens, in the form of 18 cm by 12 cm sheets of paper affixed to a metallized plastic film with an acrylic glue (susceptor) were formed into shallow trays with bottom dimensions of 14 cm by 8 cm. The paper had a basis weight of 52 mg/in^2, and was prepared with 1.0% (w/w) FCS added to the pulp slurry. (For microwave susceptor applications, the FCS would only be added at the wet-end.) The specimen trays were filled to a depth of 0.6 cm with 43 g (46 mL) of Miglyol 812 for a volume-to-surface area of 33 mL/dm^2 (2 mL/in^2). Blanks were prepared using beakers containing like quantities of Miglyol 812.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

For the Condition of Use B application, Miglyol 812, and aqueous solutions of 15% ethanol, and 3% acetic acid were used as the food simulating solvents. Test articles were extracted for two hours at 175°C (Miglyol), or four hours at 100°C (15% ethanol and 3% acetic acid). Each replicate extract contained 1.5 dm^2 (23 in^2) of specimen, and 40 mL of simulant for a volume-to-surface area of 2 mL/in^2 (27 mL/dm^2). The resulting extracts were clear in appearance, and no precipitate was observed.

For the microwave application, Miglyol 812 was used as the food simulating solvent. The specimen trays containing Miglyol were microwaved for six minutes at a power of 600 Watts. Each replicate extract contained 1.4 dm^2 (22 in^2) of specimen, and 46 mL of simulant for a volume-to-surface area of 2 mL/in^2. The resulting extracts were clear in appearance, and no precipitate was observed.

000014

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in² 0.011 mg/in² 0.021 mg/in²	0.015 mg/in²
			40°C analysis after 24 hours	0.015 mg/in² 0.014 mg/in² 0.022 mg/in²	0.017 mg/in²
			40°C analysis after 96 hours	0.017 mg/in² 0.017 mg/in² 0.023 mg/in²	0.019 mg/in²
			40°C analysis after 240 hours	0.020 mg/in² 0.021 mg/in² 0.023 mg/in²	0.021 mg/in²

000015

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Paper containing 1.5% Fluorolink® F10 added to pulp slurry	Fluorolink® F10	Miglyol 812	175°C, 2 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.5% Fluorolink® F10 added to pulp slurry	Fluorolink® F10	3% acetic acid	100°C, 4 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.5% Fluorolink® F10 added to pulp slurry	Fluorolink® F10	15% Ethanol	100°C, 4 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.5% Fluorolink® F10 added at the size press	Fluorolink® F10	Miglyol 812	175°C, 2 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.5% Fluorolink® F10 added at the size press	Fluorolink® F10	3% acetic acid	100°C, 4 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.5% Fluorolink® F10 added at the size press	Fluorolink® F10	15% Ethanol	100°C, 4 hr.	<0.00047 mg/in^2 <0.00047 mg/in^2 <0.00047 mg/in^2	<0.00047 mg/in^2
Paper containing 1.0% Fluorolink® F10 added to pulp slurry	Fluorolink® F10	Miglyol 812	600 W, 6 min.	<0.00051 mg/in^2 <0.00051 mg/in^2 <0.00051 mg/in^2	<0.00051 mg/in^2

(10.99 µg Fluorolink® F10/mL isopropanol) x (40 mL simulant/1.5 dm^2 specimen) x (1 mL isopropanol/40 mL simulant) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.00047 mg Fluorolink® F10/ in^2 specimen used for Condition of Use B testing.

(10.99 µg Fluorolink® F10/mL isopropanol) x (46 mL simulant/1.4 dm^2 specimen) x (1 mL isopropanol/46 mL simulant) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.00051 mg Fluorolink® F10/ in^2 specimen used for testing of microwave applications.

These migration results are used in Section G to calculate EDI's. While the time and temperature at which these extractions were carried out for the non-microwave application do not specifically track the recommendations in FDA's Chemistry Guidance for testing at Condition of Use B, we use the principles of diffusion as described in Part 2 of this Section and in Appendix III to demonstrate that the migration data presented above are exaggerative with respect to Condition of Use B.

000016

Section F - MIGRATION LEVELS IN FOOD - Continued

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Extract Identification	Replicate	Initial Concentration (µg/mL)	Amount Added (µg/mL)	Amount Detected (µg/mL)	Amount Recovered (µg/mL)	Recovery (%)	Mean Recovery (%)
Miglyol extract of pulp treated specimen	1	<10.99	14.66	14.2	14.2	97	98±5
	2	<10.99	14.66	15.1	15.1	103	
	3	<10.99	14.66	13.8	13.8	94	
3% acetic acid extract of pulp treated specimen	1	<10.99	14.66	10.5	10.5	94	95±0.6
	2	<10.99	14.66	11.1	11.1	95	
	3	<10.99	14.66	11.6	11.6	95	
15% ethanol extract of pulp treated specimen	1	<10.99	14.66	13.8	13.8	71	75±4
	2	<10.99	14.66	13.9	13.9	76	
	3	<10.99	14.66	13.9	13.9	79	
Miglyol extract of microwave specimen	1	<10.99	14.66	12.6	12.6	86	91±6
	2	<10.99	14.66	13.3	13.3	91	
	3	<10.99	14.66	14.2	14.2	97	

Fortification Level: (14.66 µg Fluorolink® F10/mL isopropanol) x (40 mL simulant/1.5 dm^2 specimen) x (1 mL isopropanol/40 mL simulant) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.00063 mg Fluorolink® F10/ in^2 specimen. Details are included in Appendices I and II.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

The migration testing described above for this FCS is used in conjunction with the calculations presented in Appendix III of this notification to calculate the EDI's in Section G. FDA's guidance document for conducting the migration data necessary to support an FCN recommends that, for Condition of Use B, extractions may be conducted in solvents simulating the intended types of food for 2 hours at 100°C, followed by 238 hours at 40°C. The migration studies that Solvay Solexis conducted for this FCN, however, extracted paper treated with Fluorolink® F10 for 2 hours at 175°C in Miglyol 812 and 4 hours at 100°C in 3% acetic acid and 15% ethanol. We include diffusion calculations in Appendix III to demonstrate that the extraction studies conducted by Solvay Solexis are more severe, i.e., would result in more migration, than studies conducted according to the conventional testing conditions recommended by FDA. In consideration of the results of the calculations discussed in Appendix III, we believe that the analytical testing conducted by Solvay Solexis is sufficient to accurately demonstrate the amount of migration of Fluorolink® F10 from paper and paperboard when used in contact with food at temperatures equivalent to FDA's Condition of Use B.

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Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

$$\begin{aligned} EDI &= DC \times 3 \text{ kg food/p/d} \\ &= CF \times \langle M \rangle \times 3 \text{ kg food/p/d} \\ &= CF \times [(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})] \times 3 \text{ kg/p/d} \end{aligned}$$

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The EDI calculations for Fluorolink® F10 oligomers, presented in Appendix IV, use the migration data described in Section F and Appendices I and II of this FCN. In reviewing the results of these EDI calculations, we note that they are founded in part on migration data generated under conditions more rigorous than Condition of Use B. This is discussed more fully in Section F and Appendix III of this FCN.

Summing the dietary exposures to the FCS from its use in the applications covered by this FCN, we have a CEDI (4.73 ppb dietary) only nominally greater than the EDI that FDA found acceptable for the applications described in FCN 195, covering Conditions of Use C [redacted]ugh H. The additional dietary exposure that would result from the applications covered by this FCN, that were not covered by FCN 195, is [redacted]ppb.

The EDI calculations for all other compounds that may be present in the FCS are discussed in FCN 195, Section F, which is incorporated here by reference. The estimated dietary exposure to these impurities was based on residual analyses on the diol precursor in conjunction with a calculation of 100% migration from the finished Fluorolink® F10 polymer. Thus, the EDI for these materials is not effected by the expanded applications of use covered by this FCN.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

000018

Memorandum

Date: July 14, 2004

From: Division of Food Contact Notifications, Chemistry Group I, HFS-275

AD

Subject: FCN 416: Solvay-Solexis S.p.A. via Keller & Heckman; submissions of 3/29/04 and 6/1/04. Phosphate esters of ethoxylated perfluoroether as a water and oil repellent for paper and paperboard.

To: Division of Food Contact Notifications, Regulatory Group I
Attn.: M. Hepp, Ph.D.

Solvay Solexis S.p.A. (Solvay), through their agent Keller and Heckman LLP (K&H), submitted this notification for the use of the food contact substance (FCS) identified as phosphate esters of ethoxylated perfluoroether, prepared by reaction of ethoxylated perfluoroether diol (EPFED) with phosphorous pentoxide or pyrophosphoric acid, for use as a water and oil repellent in the manufacture of paper and paperboard. The FCS is for use at a level not to exceed 1.5 wt-% under conditions of use B-H and at levels up to 1 wt-% in microwave susceptor applications.

The FCS is effectively notified for use at a level not to exceed 1.5 wt-% in paper and paperboard under conditions of use C-H as a result of FCN 195 (Solvay). Information in FCN 195 is incorporated by reference. The FCS and use are similar to those described in FCN 398 (Solvay).

The only new information in this FCN are migration studies (Appendices 1 and 2) and calculations pertaining to migration to food (Appendix 3). Information on the identity, manufacture, chemical/physical specifications and technical effect (Form 3480, Parts II.A-C) was reviewed in the chemistry review memorandum on FCN 195.[1]

As described below, the dietary concentration (DC) for oligomers of the FCS is 9 ppb, and the estimated daily intake (EDI) is 27 µg/p/d.

Identity

Information on the identity of the FCS is summarized in Part II, Sections A and C, of Form 3480 and is consistent with that given in the 2/11/02 memorandum on FCN 195 and summarized below.

Name: Phosphate esters of ethoxylated perfluoroether diol

CAS Reg. No.: 200013-65-6

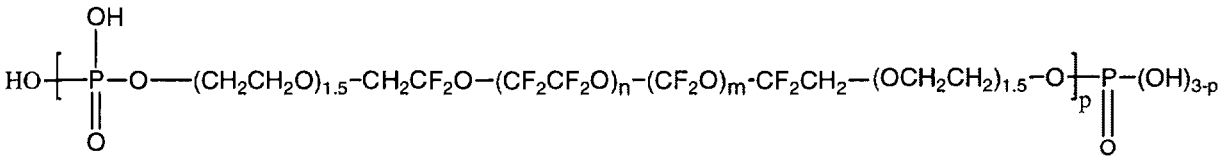
[1] D. Folmer to A. Shanklin, Memorandum on FCN 195 dated 2/11/02.

CAS Name: Diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene

Trade Name: Fluorolink F10

Molecular weight (for oxidized precursor EPFED): 1800 (M_n), 2200 (M_w)

Structure:



-where p=1 for the monoester, and p=2 for the diester (≤ 30 mol-% diester)
-values for n and m are approximately 6

Fluorolink F10 Properties

Table 1. Summary of Physical and Chemical Properties.

Property	**Value**
Functional groups	Phosphate
Color	Pale brown
Appearance	Viscous liquid
Specific gravity (20° C)	1.73 g/cm^3
Dynamic viscosity (20° C)	60,000 cps
Solubility at 25° C	
Water	Insoluble
Isopropyl alcohol	≤ 0.5 wt.%
n-hexane	Insoluble
Toluene	Insoluble
Propylene glycol	≤ 0.5 wt.%
Acetone	Insoluble
Methyl ethyl ketone	Insoluble

Characterization. Spectral data identifying the FCS is included in Appendix II of FCN 195. The notifier included an infrared (IR) spectrum of Fluorolink F10 as well as a gel permeation chromatogram (GPC) for EPFED, a precursor of the FCS. The peak at about 1250 cm^{-1} in the IR spectrum may be attributed to the stretching of the P-O double bond (P=O). The data are consistent with the molecular structure given, and adequately characterize the FCS.

We continue to have no questions on the identity of the FCS.

Manufacture

In Section II.B of Form 3480, the notifier refers to manufacturing and impurity information included in FCN 195, specifically in Appendix I (description of manufacturing process) and Appendix III (information on starting materials and precursors). As described in the 2/11/02 memorandum on FCN 195 and summarized below,

Impurities. Residue levels for TFE, EO and 1,4-dioxane (see Appendix IV of FCN 195) were determined by analysis of the polymer precursor, EPFED (see II), not the FCS. 1,4-Dioxane and EO were extracted using dimethylacetamide followed by analysis using gas chromatography-mass spectrometry (GC-MS). TFE was analyzed by means of head space analysis and gas chromatography employing a flame ionization detector (GC-FID).

Table 2. Impurity Composition

Impurity	CAS #	Residual Level
EPFED	162492-15-1	< 5 wt-%
Isobutanol (solvent)	78-83-1	< 0.3 wt-%
Phosphoric acid	7664-38-2	< 1 wt-%
Ethanol	64-17-5	< 0.1 wt-%
Acetic acid	64-19-7	< 0.2 wt-%
Tetrafluoroethylene (TFE)	116-14-3	< 28 ppb (residual level in precursor)
Ethylene oxide (EO)	75-21-8	< 240 ppb (residual level in precursor)
1,4-dioxane	123-91-1	< 1.6 ppm (residual level in precursor)

Phosphoric acid, ethanol, and acetic acid are claimed by the notifier to be generally recognized as safe (GRAS) under 21 CFR 182.1073, §184.1293, and §184.1005, respectively. The notifier claims that PFED would not be present in the FCS since all PFED would be converted to EPFED during the manufacturing process (p.7). Phosphorous pentoxide and pyrophosphoric acid would not be expected to be present in the FCS since these species would rapidly convert to phosphoric acid in the presence of water.

We have no questions on the manufacture and impurities of the FCS. We have two additional comments since review of the chemistry information in FCN 195.

Potential for PFOA Formation.[3] It is our judgment that perfluorooctanoic acid (PFOA) will not be present in the subject FCS. PFOA is not used as a starting material in the manufacture. The oxidative polymerization used to produce the FCS is such that only $-CF_2O-$ and $-CF_2CF_2O-$ units form, i.e., the maximum length of any perfluoro group in the polymer is C_2. The FCS is related to the subject of FCN 398, for which the notifier stated, "the reactivity of the fluorinated radicals towards oxygen is so high that no oligomers of TFE can be detected" (see Appendix 3, p. 27 of FCN 398). We agree that the likelihood of the formation of C_8 perfluoro groups (required to form PFOA) is essentially zero.

Low Molecular Weight Oligomers. In Section II.C.2 of Form 3480, the notifier states that the molecular weight distribution (MWD) of the FCS is expected to be similar to that of EPFED. A GPC of EPFED (Appendix II of FCN 195, also see the 12/18/01 submission to FCN 195) demonstrated that the percentage of oligomers as a function of molecular weight is as follows: ≤800 Daltons, 1.7%; ≤980 Daltons, 3.8%; ≤1030 Daltons, 5.1%. We thus will assume that the FCS contains at most 5% low molecular weight oligomers (LMWO).

[3] Adapted from K. Paquette to P. Honigfort, Chemistry memorandum on FCN 398 dated 3/23/04.

Use, Use Level, and Intended Technical Effect

In Section II.D of Form 3480, the notifier states that the FCS is intended as an oil and water repellant in the manufacture of food-contact paper and paperboard. The FCS will be added to paper and paperboard, at either the wet-end or at the size press, at a level not to exceed 1.5% by weight in the finished paper and paperboard. Paper containing the FCS at a level not to exceed:

1) 1.5% by weight of the finished paper and paperboard will be used in contact with all food types under Conditions of Use B-H. *This FCN would include condition of use B to the notified use in FCN 195.*
2) 1% by weight of the finished paper and paperboard, will be used in contact with all food types in microwave susceptor applications.

Draft language for the notification letters is contained in Appendix 5 of the FCN. Given that the proposed use subsumes that in FCN 195, the notifier may wish to withdraw FCN 195.

In Section II.D.3 of Form 3480, the notifier refers to intended technical effect information included in FCN 195. As described in the 2/11/02 memorandum on FCN 195, the FCS is intended to impart oil and water repellence to food-contact paper and paperboard. Results from two tests designed to determine oil (the Kit Test, TAPPI method 557) and water repellency (the Cobb60 test, TAPPI method T441) are included. The test results indicate increased oil or water repellence in paper as the use level was increased from 0 to 1.5 wt-% in paper.

We have no questions on the proposed use and intended technical effect of the FCS.

Migration Levels in Food

Migration studies conducted on paper samples manufactured with the FCS are summarized in Section II.F of Form 3480. The full studies are contained in Appendices 1 and 2 to the FCN. Appendix 1 contains a migration study involving conventional heating while Appendix 2 contains a migration study using microwave susceptors. Both studies were conducted by TNO Nutrition and Food Research Institute. As described in detail under Comments, we have not used the results of these studies to estimate consumer exposure.

Conventional heating. Two types of paper samples were treated with 1.5 wt.-% of the FCS, one by slurry addition (TNO code 0939/01/1235) and another by size press addition (TNO code 0939/01/1239). The paper samples were tested using 3% acetic acid and 15% ethanol (non-fatty simulant) at 100°C for 4 h and Miglyol 812 (fatty simulant) at 175°C for 2 h. Appendix 3 of the FCN contains calculations using diffusion principles to demonstrate that the testing conditions, which had no low temperature phase, were nonetheless acceptable to model condition of use B (100°C/2 h, 40°C/ 238 h). We agree with this conclusion, although, as discussed in the Estimation of Oligomer Migration section, we do not accept the notifier's method.

Test paper samples (10 cm x 15 cm) were cut into small pieces (1 cm x 3 cm) and placed in a headspace vial (50 pieces, 23 in^2 1-sided), food simulant added (40 mL), the vial closed and

heated in an oven at 100°C for 4 h (non-fatty) and 175° C for 2 h (fatty). The sample mass-to-surface area ratio was about 2 mL/in^2, an acceptable value for migration studies conducted on paper samples. At the end of each time period, the aqueous extracts were evaporated to dryness and the residues dissolved in isopropanol (1 mL), while the Miglyol extracts were extracted into a methanol-ammonia solution, evaporated to dryness, and the residues dissolved in isopropanol (1 mL). The isopropanol extracts were analyzed by high performance liquid chromatography with mass spectrometric detection (LC-MS) in the range of m/z 800-1700. The LS-MS method is described in the appendix to the TNO report. All testing was conducted in triplicate. Controls (blanks) consisted of simulants treated as above with no test samples.

A calibration curve was prepared from sequential dilution of a stock solution of the FCS in isopropanol (7.3278 mg/mL) to give standards containing 0, 10.99, 14.66, 18.32, 21.98, 25.65, 29.31, 32.48, 36.64, 43.97, 51.29, 58.62, 65.95 and 73.128 µg/mL. The calibration curve and supporting data are shown in Figures 11-12 of the TNO report. The calibration curve was constructed by summing the peak areas of all the peaks in the m/z 800-1700 range. A representative spectrum for a calibration standard is shown in Figure 10 of Appendix 1.

The FCS was not detected in any of the extracts at a reported limit of detection (LOD) of <7.3 µg/dm^2 (<0.5 µg/in^2). Using the volume of extract for LC-MS (1 mL) and the surface area (23 in^2), this corresponds to 11 µg/mL. This is actually the lowest standard concentration. Inspection of Figure 10 in the TNO study indicates that an actual LOD would be expected to be much lower. Validation studies were conducted by spiking the extracts at about 15 µg/mL which is slightly higher than the reported LOD. The recoveries were acceptable. Blank, standard, test sample and validation LC-MS results are contained in the TNO study.

Microwave heating. The test sample (TNO code 0939/01/1803) consisted of two layers of paper, manufactured with 1 wt.-% of the FCS, each bound to a metallized plastic film with an acrylic adhesive. Paper samples (18 cm x 12 cm) were folded into shallow trays and filled with Miglyol 812 (43 g, height of 0.6 cm, surface area of 21 in^2). This corresponds to a volume-to-surface area of about 2 mL/in^2. (The notifier used a 2-sided surface area rather than 1-sided). The contents were heated in a 600W microwave oven for 6 minutes. A beaker with water (90 mL) was used as an inert load.

At the end of each time period, the extracts were treated as described above, that is extraction into an ammoniacal methanol-water mixture, dissolved in IPA (1 mL) and analyzed by LC-MS. The FCS was not detected at an LOD of 11 µg/mL, corresponding to 0.5 µg/in^2. Validation studies were conducted as described above and the recoveries were acceptable. Blank, standard, test sample and validation LC-MS results are contained in the TNO study.

Comments. We have the following comments on the migration studies:

First, the mass range used for quantification in the LS-MS method for the subject FCN and FCN 195 was m/z 800-1700. We are concerned that this range would not be useful in quantification of LMWO of <1000 Daltons that are expected to be the primary migrants. To illustrate this concern by way of an example, consider Figure 3 in Appendix 1. Figure 3 is the chromatogram

and mass spectrum obtained from analysis of the 3% acetic acid extract from the paper sample with the FCS added to the pulp slurry. Inspection of the chromatogram indicates a peak near 9 minutes with a noisy baseline. The accompanying mass spectrum is also noisy and does not contain any information on quantification below 900 Daltons, the mass range at which any LMWO migrants would be expected to appear.

Furthermore, we have no information that confirms that the LC peak near 9 minutes used to quantify migration is suitable for detection of LMWO migrants. The notifier did not provide LC/MS data for a sample containing concentrated LMWO.

Also of concern is the fact that some of the blank controls have peaks in the LC region of interest (near 9 minutes). Inspection of the chromatograph of the blank in Figure 2 (Appendix 1) suggests the presence of some material in the blank that would interfere with detection of the FCS. No rationale for this observation of several peaks at the retention time of interest (~9 minutes) was contained in the TNO report. Similar peaks near 9 minutes were also observed in chromatograms of blank controls in FCN 195 (Appendix IV, figs. 7, 12, 13, 16, 17, etc.)

Estimation of Oligomer Migration. Because of our concerns with the analytical method used in the migration studies, we considered alternate methods to quantify oligomer migration. In Appendix 3, the notifier estimated diffusion coefficients for a representative oligomer (500 Da) of the FCS to demonstrate that the migration protocols used to simulate conventional heating were equivalent to or more severe than those we recommend for Conditions of Use B. However, these diffusion coefficients (2×10^{-13} cm^2/s @40°C, 5×10^{-11} cm^2/s @100°C, 5×10^{-9} cm^2/s @175°C) cannot be used to model migration of the FCS from paper because they were calculated assuming Fickian diffusion through a polymeric substrate, not paper. The calculations further assumed a diffusivity constant ($A_p = 0$) which is average for polymers but presumably quite low for paper. According to Tim Begley of the Indirect Additives Group in FDA's Division of Chemistry Research and Environmental Review, a few diffusion coefficients for paper that have been estimated were approximately 10^{-9} for "normal" temperatures.

Migration of Perfluoropolyether Oligomers from FCN 398. Rather than basing migration levels in food on the submitted migration studies or modeling, we believe that the migration behavior of a related grease-proofing agent manufactured by the same notifier can be used to estimate migration of LMWO of the FCS. The related grease-proofing agent is the subject of FCN 398, perfluoropolyether dicarboxylic acid ammonium salt (Fluorolink C10/NH_4). We believe that the migration behavior of Fluorolink C10/NH_4 may be used to estimate migration for the subject FCS for the following reasons:

1. Fluorolink C10/NH_4 is expected to have similar perfluoropolyethylether oligomers as the FCS, Fluorolink F10. Both Fluorolink compounds have the same polymer repeat unit $(CF_2\text{-}CF_2\text{-}O\text{-})_n$, albeit different end groups.

2. Fluorolink C10/NH_4 has a MW that is similar to that of the FCS (M_n 1300-2000 Daltons) while the percentage of LMWO (22 wt-%) is more than quadruple that in the FCS (<5 wt-%).

3. The ammonium carboxylate end units of C10/NH_4 would ensure good solubility in aqueous solvents, similar to the phosphate ester end groups of the FCS. In fact, Fluorolink C10/NH_4 may well migrate more readily from paper than the FCS, whose phosphate ester groups may be more tightly bound to the paper than carboxylate groups.

4. Migration testing of paper containing 1% Fluorolink C10/NH_4 into water, 3% acetic acid, and isooctane was conducted under condition of use B and analyzed by LC-MS using the full mass range of 120-2000 Da. LMWO were clearly detected under these conditions for the C10/NH_4 standards and blank controls after standard addition (see FCN 398 Appendix 7, Figs 7, 10, 13, 16-20).

Migration tests in food simulants under migration protocol B on paper treated with 1 wt-% Fluorolink C10/NH_4 were reported as follows (as taken from Table I in our 3/23/04 memorandum on FCN 398):[4]

Table 3. Migration Values for Perfluoropolyether Oligomers from Fluorolink C10/NH_4

Food Simulant	Water	3% Acetic Acid	Isooctane
Concentration in Food (mg/kg)[a]	0.14	< 0.02	< 0.02

[a]Assuming 10 g of food contact 1 in^2 of packaging material.

Although the use level of the FCS is 1.5 wt-%, whereas that of Fluorolink C10/NH_4 is 1 wt-%, we nonetheless consider the migration values reproduced in Table 3 to be a conservative estimate of the migration of the FCS under conditions of use B-H.

As described in our 3/23/04 memorandum on FCN 398, migration calculations were used to estimate migration of Fluorolink C10/NH_4 into alcoholic food, since an alcoholic food simulant was not used in the migration tests. In a similar manner, we estimated migration of oligomers of the subject FCS assuming all of the available oligomers of MW < 1000 (5 wt-% of the FCS) migrate to alcoholic foods. The calculation, which is based on a maximum concentration of 1.5 wt-% FCS in the finished paper, an average paper basis weight of 0.052 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material, follows:

$$\frac{0.05 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.015 \text{ g FCS}}{\text{g paper}} \right| \frac{0.052 \text{ g paper}}{in^2} \left| \frac{in^2}{10 \text{ g food}} \right. = 3.9 \text{ mg/kg oligomers in food}$$

Oligomer Migration under Microwave Susceptor Conditions. We used a similar calculation assuming 100% migration of LMWO, to estimate migration of oligomers from use of the FCS in microwave suspectors. Using a maximum concentration of 1.0 wt-% FCS in microwave susceptor paper, we obtained a conservative migration value of 2.6 mg/kg oligomers in food.

Consumer Exposure

The notifier's exposure estimates for the FCS are summarized in Section II.G of Form 3480. Exposure to oligomers is discussed in Appendix 4 of the FCN. The notifier determined an oligomers dietary concentration (DC) of 4.7 ppb. We will not comment on the notifier's values.

Oligomers of the FCS. We determined a DC of 9 ppb (9 µg/kg) as follows based on the migration values discussed above.

Migration values of 140 µg/kg, 20 µg/kg, 20 µg/kg, and 3900 µg/kg were used to model migration into aqueous, acidic, fatty, and low alcohol foods, respectively, for use of the FCS under conditions of use B-H. Using a consumption factor (CF) of 0.05 for paper/ paperboard treated with grease-proofing agents and the food-type distribution factors (f_t) for the uncoated paper packaging category ($f_{aq} = 0.57$, $f_{ac} = 0.01$, $f_{fat} = 0.41$, $f_{al} = 0.01$), the DC of FCS oligomers under use B-H is:

$$DC = 0.05\ CF\ [(0.57\ f_{aq})(140\ \mu g/kg) + (0.01\ f_{ac})(20\ \mu g/kg) + (0.01\ f_{al})(3900\ \mu g/kg) + (0.41\ f_{fat})(20\ \mu g/kg)] = 6.4\ ppb$$

Using the migration value of 2.6 mg/kg and a CF of 0.001 for microwave susceptor applications, the DC for microwave susceptor use is (the 100% migration estimate into alcoholic food was included in the DC above):

$$DC = 0.001\ CF\ [(0.99\ f_{aq} + f_{ac} + f_{fat})(2600\ \mu g/kg)] = 2.6\ ppb$$

The combined DC of oligomers is 6.4 ppb + 2.6 ppb = 9 ppb (9 µg/kg).

Assuming a daily diet of 3000 grams of food/p/d, the estimated daily intake (EDI) of the FCS oligomers is 27 µg/p/d.

Impurities. As stated by the notifier, migration values of residual impurities were calculated in FCN 195 under a 100% migration model. The maximum use level of the FCS remains unchanged so modification of migration levels was not necessary. Our exposure estimates for impurities, summarized in Table 4, are lower than those calculated in FCN 195. We used a more realistic CF of 0.05 for paper/paperboard containing grease-proofing agents.

Table 4. Summary of exposure estimates.

Compound	CAS Reg. No.	DC (µg/kg (ppb))	EDI (µg/p/d)
Oligomers of the FCS	(200013-65-6)	9	27
EPFED	162492-15-1	1	3
Isobutanol	78-83-1	12	35
TFE	116-14-3	Essentially Zero	Essentially Zero
EO	75-21-8	0.0009	0.003
1,4 dioxane	123-91-1	0.006	0.02

Cumulative Exposure

The current use of the FCS subsumes that in FCN 195, such that the cumulative DC and EDI (CDC and CEDI) are 9 ppb and 27 µg/p/d, respectively.

Notification Language

The language used in the acknowledgement letter dated 6/29/04 is appropriate. Given that the proposed use subsumes that in FCN 195, the notifier may wish to withdraw FCN 195.

Conclusions

The exposure calculations for oligomers of the FCS led to the determination of a dietary concentration of **9 µg/kg** (or 9 ppb) which corresponds to an EDI of **27 µg/p/d**. This is also the CEDI.

We have no questions.

Petra Turowski, Ph.D.

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Final:Pt:7/14/04

SOLVAY SPECIALTY FCN 538

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

The FCS is the ammonium salt of the polymer with the CAS name "ethene, tetrafluoro-, oxidized, polymerized, reduced."

2. CAS Registry Number

No CAS Registry No. has been assigned to the FCS. The CAS Registry No for the acidic form of the polymer is "69991-62-4."

3. Trade or Common Name

(b) (4) (b) (4)

4. Other Chemical Names (IUPAC, etc.)

Perfluoropolyether dicarboxylic acid, ammonium salt

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is the ammonium salt of perfluoropolyether dicarboxylic acid that results from the neutralization of perfluoropolyether dicarboxylic acid (CAS Registry Number 69991-62-4) with aqueous ammonia (CAS Registry Number 1336-21-6). The structure of the polymer may be represented as follows:

$$H_4N^+{}^-OOC\text{-}CF_2\text{-}(OCF_2\text{-}CF_2)_n\text{-}(OCF_2)_m\text{-}O\text{-}CF_2\text{-}COO^-NH_4^+$$

The minimum M_w and M_n specifications for the polymer are (b) , respectively.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

Typical Infra-red, and ^{19}F-NMR spectra of the FCS may be found in Attachment I of FCN 398.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
Perfluoropolyether dicarboxylic acid	69991-62-4	Polymer
Ammonium hydroxide	1336-21-6	Provides counter ion for acid moieties on the polymer
(b) (4) [redacted]		

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

CONFIDENTIAL

[redacted]s the ammonium salt of perfluorpolyether dicarboxylic acid. The acid form of perfluoropolyether dicarboxylic acid is insoluble in water; (b) (4) [redacted] Perfluoropolyether dicarboxylic acid has been assigned the CAS Registry Number 69991-62-4; a CAS registry number has not been assigned to the corresponding ammonium salt of this polymer. The material data safety sheets (MSDS) for (b) (4) [redacted], ammonium hydroxide, perfluorpolyether dicarboxylic acid, and the ammonium salt of perfluorpolyether dicarboxylic acid are found in Attachment II of FCN 398. The confidential details of the manufacturing process for perfluoropolyether dicarboxylic acid and the details concerning the formation of the ammonium salt are attached in Confidential Attachment III to FCN 398. (b) (4) [redacted]

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE - Continued

List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
(b) (4)		< 30 ppm	30 ppm (See Attachment IV, FCN 398)
		< 10 ppb	10 ppb (See Attachment IV, FCN 398)

Ensure that exposures to these substances are addressed in Section II.G of this form.

000008

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

Property	Max. Value	Min. Value	Individual Batch Values
M_w	(b) (4) [redacted]		
M_n			
Appearance			
pH			
Solids			

000009

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Approximately 22% of the polymer is oligomeric, with a molecular weight less than 1000 Daltons. Molecular weight was determined by gel permeation chromatography (GPC) on the methyl ester derivative of the polymer for ease of analysis. See Attachment V, FCN 398 for GPC data. (Fomblin Z DIAC is the tradename for the tetrafluoropolyether dicaboxylic acid polymer).

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

The FCS is intended for use as an oil and water repellant in paper and paperboard, and is added at the size press. The maximum addition rate is 1.0% of polymer by weight of dry finished paper and paperboard for fatty and acidic food contact applications. The maximum addition rate is 0.5% of polymer by weight of dry finished paper and paperboard for aqueous food contact applications. The FCS is fully substantive to the fiber and remains in the finished paper.

Suggested language for describing the FCS and the applicable limitations for its use in contact with food is proposed in Attachment 4.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

000010

Part II — CHEMISTRY INFORMATION - CONTINUED

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use
(b) (4) at a level not to exceed 0.5 weight percent in dry finished paper or paperboard as an oil and water repellant	Aqueous	B through H
(b) (4) at a level not to exceed 1.0 weight percent in dry finished paper or paperboard as an oil and water repellant	Acidic and fatty	B through H

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

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Part II — CHEMISTRY INFORMATION - CONTINUED

State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

Oil and water repellant properties are measured by the Kit Test (TAPPI Method 559), and the $Cobb_{60}$ Test (TAPPI Method 441) respectively Copies of these methods are attached in FCN 398, Attachment VI. The Kit Value represents the repellency and/or antiwicking characteristics to oil of paper and paperboard treated with fluorochemicals. The Cobb value indicates the mass of water absorbed by one square meter of paper over a specific time. Typical values for (b) (4) treated paper are as follows (Note that these values are for wet-end treated (1% FCS) paper; however, we anticipate substantively similar results from size press treated paper):

Dry weight % PT 5071	Kit Value ($g/m^2/d$)	$Cobb_{60}$ value (g/m^2)
0.4	7	50
0 6	8	40
0.8	10	35
1.0	10	30

Section E - STABILITY DATA

See Chemistry Recommendations Section II.D.2

Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis,) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None

000012

Part II — CHEMISTRY INFORMATION - CONTINUED

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure
N/A		

000013

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Test specimens, in the form of 10 cm by 15 cm paper sheets with a basis weight of 52 mg/in^2, were prepared with either 0.5%, or 1% (w/w) FCS added at the size press, depending on the simulant used.
. Similar control specimens were prepared without the addition of the FCS. Both test and control specimens were sectioned into 1 cm by 3 cm pieces, and 50 of these 3 cm^2 (0.03 dm^2) sections were added to headspace vials (1.5 dm^2 total surface area) containing 40 mL of pre-heated food simulating solvent. The headspace vials were sealed and the resulting volume to surface area was 27 mL/dm^2 (2 mL/in^2). The specimens were immersed in food simulating solvent, however, the surface area of a single side was used in calculating the volume to surface area ratio due to the fact that the specimen thickness was less than 254 µm (0.01 in). The resulting extracts were clear in appearance and no precipitate was observed.

A full report of the migration study is provided in Attachment 1.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Water, iso-octane, and a 3% aqueous solution of acetic acid were used as food simulating solvents. Prior consent for use of iso-octane as a fatty food simulant was obtained from FDA/CFSAN (tracking number CTS 84710, see Attachment VIII, FCN 398). Water, rather than 10% ethanol was selected as the simulant for aqueous foods for reasons analogous to the justification presented in the aforementioned correspondence for use of iso-octane as the fatty simulant. Specifically, the FCS is so soluble in alcohol, that the use of alcohol unreasonably exaggerates the potential migration of the FCS to aqueous and fatty foods. Because alcohol was not used as a simulant in the migration testing, and because we intend to use this FCS with all food types, we have conducted 100% migration calculations for use in the EDI determination for the exposure contribution of the FCS oligomers from alcoholic foods.

Test and control specimens were extracted in triplicate in all three food simulating solvents for 2 hr at 100°C, followed by an additional 238 hours at 40°C (Condition of Use B). It may be noted upon review of the migration testing report that in addition to extraction under FDA conditions, separate extractions in iso-octane and aqueous acetic acid were conducted for 4 hours at 60°C and 100°C, respectively, for the purpose of submitting a dossier to permit the use of the FCS for food-contact applications in the European Union. These data were not relied on for the purposes of this submission as migration data collected according to FDA's Chemistry Guidelines is available.

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Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

000015

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Paper containing 0.5% (b) (4)	(b) (4)	Water	100°C for 2 hr	0.0008 mg/in^2 0.0012 mg/in^2 0.0012 mg/in^2	0.0010 mg/in^2
Paper containing 0.5% (b) (4)		Water	100°C for 2 hr, followed by 238 hr at 40°C	0.0003 mg/in^2 0.0004 mg/in^2 0.0003 mg/in^2	0.0003 mg/in^2
Paper containing 1% (b) (4)		3% acetic acid	100°C for 2 hr	<0.0001 mg/in^2 <0.0001 mg/in^2 <0.0001 mg/in^2	<0.0001 mg/in^2
Paper containing 1% (b) (4)		3% acetic acid	100°C for 2 hr, followed by 238 hr at 40°C	<0.0001 mg/in^2 <0.0001 mg/in^2 <0.0001 mg/in^2	<0.0001 mg/in^2
Paper containing 1% (b) (4)		Iso-octane	100°C for 2 hr	<0.0001 mg/in^2 <0.0001 mg/in^2 <0.0001 mg/in^2	<0.0001 mg/in^2
Paper containing 1% (b) (4)		Iso-octane	100°C for 2 hr, followed by 238 hr at 40°C	<0.0001 mg/in^2 <0.0001 mg/in^2 <0.0001 mg/in^2	<0.0001 mg/in^2

The water extract was directly analyzed. The following calculation demonstrates conversion of aqueous concentration to migration in mg/in^2:

(0.92 µg (b) (4) /mL water) x (40 mL water/3.0 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0008 mg (b) (4) /in^2 paper.

Prior to analysis of the acetic acid and iso-octane extracts, 40 mL of extract was evaporated, and the residue taken up in 10 mL of iso-propanol (IPA), or water respectively. Concentrations are reported as µg/mL oligomer in IPA or water. The following is an example of how these values were used to calculate the corresponding migration levels in mg/in^2:

(0.51 µg (b) (4) /mL IPA) x (40 mL acetic acid/3.0 dm^2 specimen) x (10 mL IPA/40 mL acetic acid) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0001 mg (b) (4) /in^2 paper.

000016

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

[redacted] Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Extract Identification	Replicate	Fortification Level (µg/mL)[a]	Amount Detected (µg/mL)	Recovery (%)	Mean Recovery (%)
240 hr. iso-octane extracts of FCS treated paper	1	0.12	0.11	87	85±18
	2	0.12	0.13	103	
	3	0.12	0.08	66	
240 hr. acetic acid extracts of FCS treated paper	1	0.12	0.12	100	92±16
	2	0.12	0.13	103	
	3	0.12	0.09	73	

a. Level 1 Fortification: (0.12 µg [redacted] (b) [redacted]/mL simulant) x (40 mL simulant/3.0 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0001 mg [redacted] (b) [redacted]/in^2 paper.

Extract Identification	Replicate	Initial Concentration (µg/mL)	Amount Added (µg/mL)	Amount Detected (µg/mL)	Amount Recovered (µg/mL)	Recovery (%)	Mean Recovery (%)
240 hr water extracts of FCS treated paper	1	0.35	0.32[b]	0.62	0.27	84	87±2
	2	0.40	0.32	0.68	0.28	88	
	3	0.33	0.32	0.61	0.28	88	

[redacted] b. Fortification: (0.32 µg [redacted] (b) [redacted]/mL simulant) x (40 mL simulant/3.0 dm^2 specimen) x (0.1 dm/cm)^2 x (2.54 cm/in)^2 x (0.001 mg/µg) = 0.0003 mg [redacted] (b) [redacted]/in^2 paper.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

Substance	100% Migration (ppb)
(b) (4) [redacted]	7.5
	0.0025
Oligomers	11,000 (migration to alcoholic foods)

[redacted] Please see Attachment 2 for complete details

000017

Part II — CHEMISTRY INFORMATION - CONTINUED

Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Migration of the FCS oligomers in acidic and fatty simulants at all timepoints is less than the method limit of detection (LOD) of 0.0001 mg/in^2 (10 ppb, 10 µg/kg in food). In aqueous simulant, a maximum migration of 0.00120 mg/in^2 (120 ppb, 120 µg/kg) is measured. The contribution to the EDI of oligomers extractable in an alcoholic simulant was estimated using a 100% migration calculation (below). The weighted migration <M> is calculated using the 100% migration value for alcoholic foods, the LOD as the migration value for acidic and fatty foods, the measured migration for aqueous foods, and food type distribution factors (f_T) of 0.57, 0.01, 0.01, and 0.41 for aqueous, acidic, alcoholic, and fatty foods respectively:

<M> = $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$
= [(120 µg/kg)(0.57) + (10 µg/kg)(0.01) + (11,000 µg/kg)(0.01) + (10 µg/kg)(0.41)]
= [68 µg/kg + 0.1 µg/kg + 110 µg/kg + 4.1 µg/kg]
= 182 µg/kg (182 ppb in food).

The EDI is then calculated using a consumption factor (CF) of 0.1 for uncoated and clay coated paper:

EDI = <M> x CF
= 182 µg/kg x 0.1
= 18.2 µg/kg (18 ppb in the diet)

Substance	Dietary exposure (ppb)
Oligomers	18.2
(b) (4) [redacted]	0.75
	0.00025

Please see Attachment 3 for complete details of the (b) (4) [redacted] exposure calculations.

000018

Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

Memorandum

Date: October 31, 2005

From: Division of Food Contact Notifications
Chemistry Group I, HFS-275

Subject: FCN 538: Solvay Solexis S.p.A., through Keller & Heckman; submissions of 7/20/05 and 10/28/05. Perfluoropolyether dicarboxylic acid, ammonium salt, as a grease-proofing agent for paper/paperboard applied at the size press.

To: Division of Food Contact Notifications
Regulatory Group II, HFS-275
Attn: P. Honigfort, Ph.D.

Keller & Heckman (K&H), on behalf of Solvay Solexis, has submitted a food contact notification (FCN) to allow perfluoropolyether dicarboxylic acid, ammonium salt (trade name [redacted]) to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard intended to contact acidic and fatty foods (although K&H's exposure estimate included a substantial contribution from use in contact with alcoholic foods; see below) and at levels up to 0.5 wt-% in dry finished paper/paperboard intended to contact aqueous foods, all under conditions of use B through H. The food-contact substance (FCS) will be added at the size press during paper manufacture. This FCS is the subject of effective FCN 398 (Solvay Solexis) for use prior to the sheet-formation process at levels up to 1 wt-% in dry finished paper/paperboard intended to contact all types of food under conditions of use B through H.

IDENTITY, MANUFACTURE, COMPOSITION, AND STABILITY

These data are summarized in the Chemistry memorandum for FCN 398, which is attached.[1] As was discussed in FCN 398, [redacted] will not be present in the subject FCS.

In FCN 398, the typical residual levels of two potential impurities, [redacted] and [redacted], were determined to be < 10 µg/kg and < 30 mg/kg, respectively, in the finished [redacted] (suspension containing 20 wt-% FCS solids).

Adequate gel permeation chromatography (GPC) data were provided in FCN 398 to demonstrate that the concentration of oligomers of molecular weight (MW) < 1000 Daltons is 22 wt-% of the FCS.[1]

[1] FCN 398, memorandum dated 3/23/04, K. Paquette to P. Honigfort.

INTENDED USE AND USE LEVEL

The subject FCN proposes to allow (b) (4) to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard in paper and paperboard intended to contact acidic and fatty foods and at levels up to 0.5 wt-% in dry finished paper/paperboard intended to contact aqueous foods, all under conditions of use B through H. The FCS will be added at the size press. The FCS is fully substantive to the fiber and will remain in the finished paper. Because K&H's exposure estimate included a substantial contribution from a 1 wt-% use level of the FCS in paper intended to contact alcoholic foods (see Part II.F.2 and II.G.1 of Form 3480 and Attachment 2 to the FCN), we asked K&H to clarify the intended uses. K&H responded on 10/28/05 that the subject FCN should include use of paper treated with the FCS in contact with alcoholic foods.[2]

Typically, grease-proofing agents are not added at both the wet end and size press during papermaking due to the technically limited effect of the FCS and the high cost of perfluoropolymer grease-proofing agents. In fact, grease-proofing agents are added primarily at the size press to prevent losses that occur during wet-end processing.[3] We therefore asked K&H to clarify whether the maximum use levels described for the FCS in the subject FCN and in FCN 398 are the total concentration of the FCS in finished paper whether the FCS is added at the wet end or the size press. K&H verified that they are and agreed to combine the uses described in FCNs 538 and 398 into the subject FCN with a single maximum use level of 1 wt-% of the FCS in finished paper (0.5 wt-% if the FCS is added at the size press and the paper is used in contact with aqueous foods).[2]

TECHNICAL EFFECT

The technical effect data provided in FCN 398 support the intended uses described in the subject FCN.[1]

MIGRATION DATA FOR TOTAL OLIGOMERS (Attachment 1, summary in Part II.F.1 of Form 3480)

Migration tests on paper treated with (b) (4) were conducted by TNO Quality of Life, Netherlands, into water, 3% acetic acid, and isooctane to simulate condition of use B (100° C for 2 hr followed by 40° C for 10 d). TNO stated that the high solubility of the FCS in aqueous ethanol mixtures would yield exaggerated migration results, hence TNO's use of water, 3% acetic acid, and isooctane as food simulants. We have accepted isooctane as a fatty-food simulant on several occasions in the past and specifically allowed its use in FCN 398.[1]

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[2] E-mail dated 10/28/05, D.W. Hill (K&H) to E. Machuga (HFS-275).
[3] Meeting between the American Forestry and Paper Association (AFPA) and FDA on 12/9/03.

Total oligomers were determined in these studies via liquid chromatography with mass spectrometric detection (LC/MS) with limits of detection (LOD) of 0.51 μg/mL in isooctane, 0.48 μg/mL in 3% acetic acid, and 0.06 μg/mL in water, each in the sample injected into the instrument (see p. 48 of Attachment 1 to the FCN). This same method was used and validated in FCN 398. TNO has provided adequate sample and validation data, chromatograms, and calibration curves to support the migration measurements reported in Attachment 1 to the subject FCN. In the spike-and-recovery validation experiments, the average percent recovery values were acceptable for concentrations > 0.1 mg/kg (μg/mL) in the food simulants: 89% in isooctane, 94% in 3% acetic acid, and 87% in water.[4] Although the relative standard deviation (r.s.d.) values for recoveries from isooctane (23%) and 3% acetic acid (18%) exceeded our recommended values, oligomers were not detected in any of these samples, and the spiking level in both cases was 0.12 μg/mL, which is below the LODs in these food simulants. The r.s.d. for spike-and-recovery measurements in the water food simulant was 3%, which meets our recommended value. The migration test results are summarized in Table 1.

Table 1. Migration Values for Perfluoropolyether Oligomers from the FCS

Food Simulant	Test Conditions Yielding Maximum Migration	Conc. in Analyzed Migration Sample (μg/mL)	Migration Value (μg/in^2)	Conc. in Food (μg/kg)[a]
Water	2 hr at 100° C	1.40[b]	2.4	240
3% Acetic Acid	2 hr at 100° C followed by 10 d at 40° C	< 0.48[c]	< 0.21	< 21
Isooctane	"	< 0.51[c]	< 0.22	< 22

[a]Assuming 10 g of food contact 1 in^2 of packaging material.
[b]K&H used the highest of three replicate values rather than the average, most likely due to the high r.s.d. of the replicates (21%).
[c]Oligomers were not detected under any testing conditions.

For the migration studies, paper samples of basis weight 0.052 g/in^2 were prepared by the addition of 1 wt-% of the FCS (for the isooctane and acetic acid food simulants) or 0.5 wt-% (for the water food simulant), based on the weight of the dry finished paper, at the size press. Each sample, consisting of a one-sided surface area of 23.2 in^2 (1.5 dm^2), was cut into small pieces and placed in a crimp-top vial with 40 mL of preheated food simulant for a volume-to-surface area ratio of 1.7 mL simulant/in^2. Although this value is significantly lower than our recommended 10 mL simulant/in^2, the facts that 1) the migration samples were "clear in appearance and no precipitate was observed" (see Part II.F.1.a of Form 3480), and 2) the spike-and-recovery validation experiments resulted in acceptable recoveries of the FCS spiked into the migration samples, demonstrate that the migration samples did not become saturated with the oligomers.

[4] Several of the percent recovery and r.s.d. values were calculated incorrectly by TNO. The values discussed in this memorandum are the corrected values.

The water samples were analyzed directly, while the 3% acetic acid and isooctane samples were evaporated to dryness and redissolved into 10 mL isopropanol and water, respectively, prior to analysis. An example calculation of the migration value (mg/in^2) for the oligomers in water follows:

$$\frac{1.40 \times 10^{-6} \text{ g oligomer}}{\text{g water}} \left| \frac{40 \text{ g water}}{23.2 \text{ in}^2 \text{ paper}} \right. = 2.4 \ \mu g/in^2$$

For the other simulants, the result was divided by a factor of 4 (40 mL/10 mL) to account for the preconcentration step.

Although K&H stated in Part II.F.1.a of Form 3480 that the surface area of a single side was used in calculating the volume-to-surface area ratio of the food simulant and the paper samples used in the migration studies, due to the fact that the specimen thickness was < 254 µm (0.01 in), the double-sided surface area of the paper samples (3 dm^2 or 46.4 in^2) was actually used in the migration calculations (see Part II.F.1.c of Form 3480 and pp. 6-8 of Attachment 1 to the FCN). K&H were correct that the single-sided surface area should have been used in migration calculations. Our migration values are therefore twice those reported by K&H in Part II.F.1.c of Form 3480.

EXPOSURE ESTIMATES

A. 100% Migration Calculations (Attachment 2, summary in Part II.F.2 of Form 3480)

Oligomers into Alcoholic Food Simulant

Because an alcoholic food simulant was not used in the migration tests, K&H assumed 100% migration of the oligomers of MW < 1000 determined by GPC (22 wt-% of the FCS) for the contribution of alcoholic foods to the total exposure to the oligomers. The calculation, which is based on a maximum concentration of 1 wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material, follows:

$$\frac{0.22 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.01 \text{ g FCS}}{\text{g paper}} \right| \frac{0.05 \text{ g paper}}{\text{in}^2} \left| \frac{\text{in}^2}{10 \text{ g food}} \right. = 11 \text{ mg/kg oligomers in food}$$

Residual Impurities

K&H used the residual levels of [redacted] given in the "Identity, Manufacture, Composition, and Stability" section above to calculate 100% migration values for these impurities (see Attachment 2). The following is an example calculation for [redacted], using the typical 20 wt-% solids value given in the "Identity, Manufacture, Composition, and Stability" section above for the concentration of the FCS in the [redacted] suspension, a maximum concentration of 1

wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material:

$$\frac{10\ \text{ng}\ \boxed{(b)(4)}}{\text{g}\ \boxed{(b)(4)}} \times \frac{1\ \text{g}\ \boxed{(b)(4)}}{0.20\ \text{g FCS}} \times \frac{0.01\ \text{g FCS}}{\text{g paper}} \times \frac{0.05\ \text{g paper}}{\text{in}^2} \times \frac{\text{in}^2}{10\ \text{g food}} = 2.5\ \text{ng/kg}\ \boxed{(b)(4)}\ \text{in food}$$

K&H used this value for all requested uses of the FCS even though the use level intended for paper contacting aqueous foods is 0.5 wt-%. We calculated the 100% migration value for the 0.5 wt-% use level as well (1.25 ng/kg $\boxed{(b)(4)}$ in food) so that we could refine the exposure estimate by using the two 100% migration values with the appropriate food-type distribution factors.

The results of all the 100% migration calculations are shown in Table 2.

Table 2. Concentrations of FCS Components in Food, Assuming 100% Migration

Component		Conc. in Food
Oligomers (for alcoholic food contribution only)		11 mg/kg
$\boxed{(b)(4)}$	Aq	1.25 ng/kg
	Ac, Al, Fat	2.5 ng/kg
	Aq	3.75 µg/kg
	Ac, Al, Fat	7.5 µg/kg

B. Exposure Calculations (Attachment 2, summary in Part II.G.1 of Form 3480)

K&H has correctly calculated the exposures to the components of the subject $\boxed{(b)(4)}$ $\boxed{(b)(4)}$ based on the migration data provided by TNO for oligomers in aqueous, acidic, and fatty foods, and assuming 100% migration of the oligomers into alcoholic foods and of $\boxed{(b)(4)}$ into all foods. We note, however, that we have traditionally used a consumption factor (CF) of 0.05 for paper/paperboard treated with grease-proofing agents, rather than the CF of 0.1 that K&H used for uncoated paper.[5] In addition, the measured migration values used by K&H in the calculation were half what they should have been due to the use of a double-sided paper surface area in the migration calculations. We will use the CF of 0.05, the food-type distribution factors (f_T) given in our "Recommendations" for uncoated paper, and the migration values given in Tables 1 and 2 above to calculate the dietary concentration (DC) and estimated daily intake (EDI) of the oligomers:

$$\text{DC} = 0.05\ \text{CF}\ [(0.57\ f_{aq})(240\ \mu\text{g/kg}) + (0.01\ f_{ac})(21\ \mu\text{g/kg}) + (0.01\ f_{al})(11\ \text{mg/kg}) + (0.41\ f_{fa})(22\ \mu\text{g/kg})] = 12.8 \times 10^{-9}\ \text{g oligomers/g food} = 13\ \text{ppb}$$

$$\text{EDI} = (12.8 \times 10^{-9}\ \text{g oligomers/g food})(3000\ \text{g food/p/d}) = 38\ \mu\text{g/p/d}$$

[5] See, for example, FCN 59, memorandum dated 8/1/00, R. Costantino to E. Machuga.

An example exposure calculation for [redacted], using the 100% migration values given in Table 2, follows:

DC = (0.05 CF) [(0.57 f_{aq})(1.25 ng/kg) + (0.01 f_{ac} + 0.01 f_{al} + 0.41 f_{fa})(2.5 ng/kg)]
= 0.089 pptr

EDI = (0.089 × 10^{-12} g [redacted]/g food)(3000 g food/p/d) = 0.27 ng/p/d

The exposures to the components of [redacted] are summarized in Table 3.

Table 3. Exposures to Components of [redacted]

Substance	CAS Reg. No.	Function	DC	EDI
Total oligomers		FCS itself	13 ppb	38 µg/p/d
[redacted]	[redacted]	Monomer	< 0.089 pptr[a]	< 0.27 ng/p/d
		Impurity	< 0.27 ppb[b]	< 0.80 µg/p/d

[a]Below the LOD.
[b]Detected but below the LOQ.

C. Cumulative Exposures

Because the notifier has agreed to combine FCNs 538 and 398 and establish a single maximum use level of 1 wt-% of the FCS in finished paper (0.5 wt-% if the FCS is added at the size press and the paper is used in contact with aqueous foods), the uses described in the two FCNs are substitutional for each other. Therefore, the cumulative exposures are the higher of the two sets of exposures described in FCNs 538 and 398: 13 ppb CDC (38 µg/p/d CEDI) for the total oligomers (FCN 538), < 0.12 pptr CDC (< 0.36 ng/p/d CEDI) for [redacted] (FCN 398), and < 0.38 ppb CDC (< 1.1 µg/p/d CEDI) for [redacted] (FCN 398).[1]

In FCN 398, we calculated an EDI of 3 mg/p/d for [redacted]

The CEDI for [redacted] will not increase over that determined in FCN 398 and will remain a factor of 3000 less than the EDI determined for [redacted]

NOTIFICATION LETTERS

Because the notifier has 1) agreed to combine FCNs 538 and 398 and establish a single maximum use level of 1 wt-% of the FCS in finished paper (0.5 wt-% if the FCS is added at the size press and the paper is used in contact with aqueous foods), and 2) decided to include use of the FCS in paper intended to contact alcoholic foods, FCN 398 should be withdrawn, and the "Intended Use" and "Limitations/Specifications" sections in the final letter should be written as follows:

Intended Use

As an oil and water repellent employed either prior to the sheet-forming operation or at the size press.

Limitations/Specifications

The FCS may be used at a level not to exceed 1 percent by weight of the finished dry paper and paperboard intended for use in contact with all food types. If the FCS is applied at the size press, the total use level of the FCS may not exceed 0.5 percent by weight of the finished dry paper and paperboard intended for use in contact with aqueous foods. Paper and paperboard containing the FCS are to be used under conditions of use B through H as described in §176.170(c), Table 2.

CONCLUSIONS

The exposures to the components of (b) (4) from its use as an oil and water repellent applied at the size press are summarized in Table 3 above. The cumulative exposure to the total oligomers of the FCS will increase from 9.9 ppb DC (30 μg/p/d EDI) in FCN 398 to 13 ppb DC (38 μg/p/d EDI) as a result of the new uses of the FCS. The cumulative exposures to the impurities (b) (4) will not increase. It is our judgment that (b) (4) will not be present in the subject FCS.

We have no questions.

(b)(6)

Kristina E. Paquette, Ph.D.

HFS- 245 (Begley); Chemistry Reading File
HFS-275:KEPaquette:436-1232:FCN538.doc:kep:10/27/05
Init: AABailey 10/31/05
Final:kep:10/31/05

Memorandum

Date: March 23, 2004

From: Division of Food Contact Notifications
Chemistry Group I, HFS-275

Subject: FCN 398: Solvay-Solexis S.p.A., through Keller & Heckman; submissions of 12/11/03 and 1/26/04. Perfluoropolyether dicarboxylic acid, ammonium salt, as a grease-proofing agent for paper/paperboard.

To: Division of Food Contact Notifications
Regulatory Group II, HFS-275
Attn: P. Honigfort, Ph.D.

Keller & Heckman (K&H), on behalf of Solvay-Solexis, has submitted a food contact notification (FCN) to allow perfluoropolyether dicarboxylic acid, ammonium salt (trade name (b) (4) [redacted] to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard intended to contact all types of food under conditions of use B through H. The food-contact substance (FCS) will be added prior to the sheet-forming process. The FCS is not currently authorized for any uses in or on food.

IDENTITY, MANUFACTURE, AND COMPOSITION

A. Identity

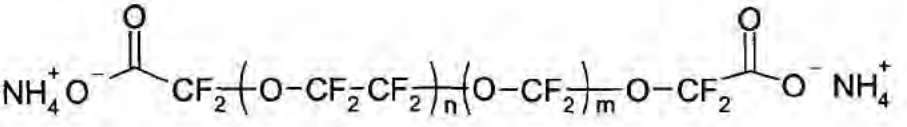
Chemical Name and CAS Registry No.

ammonium salt of ethene, tetrafluoro-, oxidized, polymerized, reduced

CAS Reg. No. for the acid form of the FCS: 69991-62-4

Common Names perfluoropolyether dicarboxylic acid ammonium salt
(b) (4) [redacted]
Fluorolink C10/NH_4

Structure



Molecular Weight

M_w (b) (4)
M_n (b) (4)
(b) < (b)

(See Part II.C.2 of Form 3480 and Appendix 5, pp. 64-71 of the FCN for supporting gel permeation chromatography (GPC) data.)

Physical Properties/Specifications

Appearance	(b) (4)
pH	(b) (4)
% Solids	(b) (4)
Density	(b) (4)
Water Solubility	(b) (4)

See Part II.C.2.a of Form 3480; Appendix 2, p. 21; and Appendix 5, pp. 72-79 for supporting data.

Data to Characterize the FCS

IR and ^{19}F NMR spectra of three production batches of the FCS are provided in Appendix 1 of the FCN.

The FCS is adequately identified.

B. Manufacture (Part II.B.2 of Form 3480 and Appendix 3 to the FCN)

(b) (4)

(b) (4) [redacted]

K&H has adequately described the manufacture of the FCS.

Potential for (b) (4) [redacted]

It is our judgment that (b) (4) [redacted] will not be present in the subject FCS. (b) (4) [redacted] We agree with the notifier that the likelihood of the (b) (4) [redacted] is essentially zero.

C. Composition

Two potential impurities, [redacted] and their typical residual levels in the finished (b) (4) [redacted] (suspension containing (b) (4) [redacted] FCS solids) are listed in Part II.B.3 of Form 3480. For (b) (4) [redacted], adequate analytical data were provided (Appendix 4, pp. 32-45) to support the < 10 µg/kg residual level determined in three production batches of the (b) (4) [redacted] suspension by headspace gas chromatography with flame ionization detection. (b) (4) [redacted] was not detected in any of the samples. For (b) (4) [redacted], however, K&H provided only a description of the ion chromatography method used (see Appendix 4, pp. 59-63) to support their claim that the (b) (4) [redacted] levels in the (b) (4) [redacted] suspension are < 30 mg/kg. In response to our 1/21/04 deficiency letter, K&H provided highly detailed raw data, chromatograms, calculations, and validation data in their 1/26/04 submission to demonstrate that the (b) (4) [redacted] levels in three production batches of the (b) (4) [redacted] suspension were < 30 mg/kg, the limit of quantification (LOQ) of the method. (b) (4) [redacted] was detected in each of the samples, but the levels were below the LOQ (see chromatograms 42, 43, and 44 at the end of the 1/26/04 submission).

Adequate GPC data for three production batches of the FCS (i.e., the solids portion of the (b) (4) [redacted] suspension) were provided in Appendix 5 to demonstrate that the concentration of oligomers of MW (b) (4) [redacted] is 22 wt-%. This value was used to calculate exposure to the FCS from use in contact with alcoholic foods (see below).

Based on the fact that the free acid precursor (b) (4) [redacted] is neutralized with ammonium hydroxide, a reaction that goes to 100% completion, exposure to (b) (4) [redacted] will be essentially zero. Since (b) (4) [redacted] is not soluble in water, any that might be present in the

FCS would not go into solution during papermaking and would therefore not be retained on the paper.

Based on the manufacturing information provided in Appendix 3 (see especially p. 31), we do not expect any additional impurities to be present in the subject FCS.

The impurities are adequately described.

D. Stability

The FCS is not expected to degrade under the intended conditions of use (see Part II.E of Form 3480).

INTENDED USE AND USE LEVEL

The subject FCN proposes to allow (b) (4) to be used as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard in paper and paperboard intended to contact all types of food under conditions of use B through H. The FCS will be added prior to the sheet-forming process. The FCS is fully substantive to the fiber and will remain in the finished paper.

TECHNICAL EFFECT

Adequate technical effect data to support use of the FCS as an oil and water repellent are provided in Part II.D.3 of Form 3480 and in Appendix 6. The standard TAPPI (Technical Association of the Pulp and Paper Industry) "Kit" and "Cobb" tests were used to demonstrate increasing grease resistance and decreasing water absorptiveness, respectively, with increasing concentrations of the FCS in paper.

MIGRATION DATA FOR TOTAL OLIGOMERS (Appendix 7, summary in Part II.F.1 of Form 3480)

Migration tests on paper treated with (b) (4) were conducted by (b) (4) into water, 3% acetic acid, and isooctane to simulate condition of use B (100° C for 2 hr followed by 40° C for 10 d). (b) (4) stated that the high solubility of the FCS in aqueous ethanol mixtures would yield exaggerated migration results, hence (b) (4) use of water, 3% acetic acid, and isooctane as food simulants. We have accepted isooctane as a fatty-food simulant on several occasions in the past and specifically allowed its use for the subject FCN (see Appendix 8 of the FCN and CTS 84710, memorandum dated 7/10/03, R. Costantino to P. Honigfort).

Total oligomers were determined in these studies via liquid chromatography with mass spectrometric detection (LC/MS). The retention time of the single analyte peak for the FCS

varied within the range 1.4 to 2.6 min, depending on the food simulant. The entire mass range of m/z 120-2000 was used to quantify the total oligomers comprising the analyte peak. (b) (4) has provided adequate sample and validation data, chromatograms, calibration curves, and calculations to support the migration measurements reported. Although raw peak areas were not provided for the water samples, we believe that the high level of detail in the description of the analytical method and in the other data support (b) (4) results for the water samples. The migration test results are summarized in Table 1.

Table 1. Migration Values for Perfluoropolyether Oligomers from the FCS

Food Simulant	Test Conditions Yielding Maximum Migration	Conc. in Analyzed Migration Sample (mg/L)[a]	Migration Value (mg/in^2)	Conc. in Food (mg/kg)[b]
Water	2 hr at 100° C	0.83	0.0014[c]	0.14
3% Acetic Acid	2 hr at 100° C followed by 10 d at 40° C	< 0.48[d]	< 0.0002	< 0.02
Isooctane	"	< 0.51[d]	< 0.0002	< 0.02

[a]Average value for three replicate samples.
[b]Assuming 10 g of food contact 1 in^2 of packaging material.
[c]K&H erred in calculating 0.0017 mg/in^2 as the average of 0.0019, 0.0012, and 0.0012 mg/in^2.
[d]Oligomers were not detected under any testing conditions.

For the migration studies, paper samples of basis weight 0.052 g/in^2 were prepared by the addition of 1 wt-% of the FCS, based on the weight of the dry finished paper, to the pulp slurry. Each sample, consisting of a one-sided surface area of 23.2 in^2 (1.5 dm^2), was cut into small pieces and placed in a crimp-top vial with 40 mL of preheated food simulant for a volume-to-surface area ratio of 1.7 mL simulant/in^2. Although this value is significantly lower than our recommended 10 mL simulant/in^2, the facts that 1) the migration samples were "clear in appearance and no precipitate was observed" (see Part II.F.1.a of Form 3480), and 2) that the spike-and-recovery validation experiments resulted in recoveries of 72 to 101% of the FCS spiked into the migration samples, demonstrate that the migration samples did not become saturated with the oligomers.

The water samples were analyzed directly, while the 3% acetic acid and isooctane samples were evaporated to dryness and redissolved into 10 mL isopropanol and water, respectively, prior to analysis. An example calculation of the migration value (mg/in^2) for the oligomers in water follows:

$$\frac{0.83 \times 10^{-6} \text{ g oligomer}}{\text{g water}} \left| \frac{40 \text{ g water}}{23.2 \text{ in}^2 \text{ paper}} \right. = 0.0014 \text{ mg/in}^2$$

For the other simulants, the result was divided by a factor of 4 (40 mL/10 mL) to account for the preconcentration step.

The limits of detection (LOD) of the LC/MS method were 0.48 mg/L for 3% acetic acid, 0.51 mg/L for isooctane, and 0.22 mg/L for water. The LODs for acetic acid and isooctane were based on the lowest standard concentration used to construct the calibration curve. The LOD for water was based on the "Within Laboratory Detection Limit," which was twice as high as the lowest standard concentration used to construct the calibration curve. (b) (4) apparently used this higher LOD to account for the variability of the water measurements.

EXPOSURE ESTIMATES

A. 100% Migration Calculations (Appendix 9, summary in Part II.F.2 of Form 3480)

Oligomers into Alcoholic Food Simulant

Since an alcoholic food simulant was not used in the migration tests, K&H assumed 100% migration of the oligomers of MW (b) (4) determined by GPC (22 wt-% of the FCS) for the contribution of alcoholic foods to the total exposure to the oligomers. The calculation, which is based on a maximum concentration of 1 wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material, follows:

$$\frac{0.22 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.01 \text{ g FCS}}{\text{g paper}} \right| \frac{0.05 \text{ g paper}}{\text{in}^2} \left| \frac{\text{in}^2}{10 \text{ g food}} \right. = 11 \text{ mg/kg oligomers in food}$$

Residual Impurities

K&H used the residual levels of (b) (4) given in the "Composition" section above to correctly calculate 100% migration values for these impurities (see Appendix 9). The following is an example calculation for (b) (4), using the typical 20 wt-% solids value given in the "Physical Properties/Specifications" section above for the concentration of the FCS in the (b) (4) suspension, a maximum concentration of 1 wt-% FCS in the finished paper, an average paper basis weight of 0.05 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material:

$$\frac{10 \text{ ng (b) (4)}}{\text{g (b) (4)}} \left| \frac{1 \text{ g (b) (4)}}{0.20 \text{ g FCS}} \right| \frac{0.01 \text{ g FCS}}{\text{g paper}} \left| \frac{0.05 \text{ g paper}}{\text{in}^2} \right| \frac{\text{in}^2}{10 \text{ g food}} = 2.5 \text{ ng/kg (b) (4) in food}$$

The results of all the 100% migration calculations are shown in Table 2.

Table 2. Concentrations of FCS Components in Food, Assuming 100% Migration

Component	Conc. in Food
Oligomers (for alcoholic food contribution only)	11 mg/kg
(b) (4) [redacted]	2.5 ng/kg
[redacted]	7.5 µg/kg

B. Exposure Calculation (Appendix 9, summary in Part II.G.1 of Form 3480)

K&H has correctly calculated the exposures to the components of the subject (b) (4) [redacted], based on the migration data provided by (b) [redacted] for oligomers in aqueous, acidic, and fatty foods, and assuming 100% migration of the oligomers into alcoholic foods and of (b) [redacted] into all foods. We note, however, that we have traditionally used a consumption factor (CF) of 0.05 for paper/paperboard treated with grease-proofing agents, rather than the CF of 0.1 that K&H used for uncoated paper.[1] We will use the CF of 0.05, the food-type distribution factors (f_T) given in our "Recommendations" for uncoated paper, and the migration values given in Tables 1 and 2 to calculate the dietary concentration (DC) and estimated daily intake (EDI) of the oligomers:

DC $= 0.05\ CF\ [(0.57\ f_{aq})(0.14\ mg/kg) + (0.01\ f_{ac})(0.02\ mg/kg) + (0.01\ f_{al})(11\ mg/kg) + + (0.41\ f_{fa})(0.02\ mg/kg)] = 9.9\ ppb$

EDI $= (9.9 \times 10^{-9}\ g\ oligomers/g\ food)(3000\ g\ food/p/d) = 30\ \mu g/p/d$

An example exposure calculation for (b) [redacted], using the 100% migration value given in Table 2, follows:

DC $= (0.05\ CF)(\Sigma f_T = 1)(2.5\ ng/kg) = 0.00012\ ppb$
EDI $= (1.2 \times 10^{-13}$ g (b) [redacted] /g food)(3000 g food/p/d) = 0.36 ng/p/d

The exposures to the components of Fluorolink PT 5071 are summarized in Table 3.

Table 3. Exposures to Components of Fluorolink PT 5071

Substance	CAS Reg. No.	Function	DC (ppb)	EDI
Total oligomers		FCS itself	9.9	30 µg/p/d
(b) (4) [redacted]		Monomer	< 0.00012[a]	< 0.36 ng/p/d
		Impurity	< 0.38[b]	< 1.1 µg/p/d

[a]Below the LOD.
[b]Detected but below the LOQ.

[1] See, for example, FCN 59, memorandum dated 8/1/00, R. Costantino to E. Machuga.

C. Cumulative Exposures

The only component of [redacted] with a potential cumulative exposure issue is [redacted] we can calculate the EDI of [redacted]

EDI = [redacted] = 3 mg/p/d [redacted]

The EDI for [redacted] determined for the subject FCS is a factor of 3000 less than that determined for [redacted] It is our judgment that use of the subject FCS will not increase the cumulative exposure [redacted] from the daily diet.

ACKNOWLEDGMENT LETTER

The acknowledgment letter dated 2/13/04 is acceptable as written.

CONCLUSIONS

The exposures to the components of [redacted] from its use as an oil and water repellent at levels up to 1 wt-% in dry finished paper/paperboard in paper and paperboard intended to contact all types of food under conditions of use B through H are summarized in Table 3 above. The cumulative exposure to [redacted] will not increase from use of this FCS. It is our judgment that PFOA will not be present in the subject FCS.

We have no questions.

Kristina E. Paquette, Ph.D.

HFS-205 (Kuznesof); 245 (Begley); Chemistry Reading File
HFS-275:KEPaquette:418-3020:FCN398.doc:kep:3/22/04
Init: AABailey 3/23/04
Final:kep:3/23/04

[2] [redacted]

SOLVAY SPECIALTY FCN 962

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene

2. CAS Registry Number

[redacted]

3. Trade or Common Name

(b) (4) [redacted]

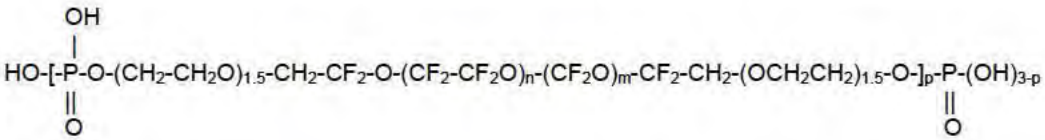
4. Other Chemical Names *(IUPAC, etc.)*

Phosphate ester of ethoxylated perfluoroether diol

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is the same material as is the subject of FCN Nos. 195 and 416. A description is presented again below for FDA's reference.



where p=(b) for the monoester, p (b) for the diester, and n and m are approximately (b)

The M_w and M_n for the polymer are typically (b) (4) [redacted], respectively.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

A characteristic IR spectrum of the FCS may be found in FCN No. 195 Appendix II.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
Ethoxylated perfluoroether diol	Not assigned	Polymer	☒ Yes ☐ No
Water	7732-18-5	Solvent	☐ Yes ☒ No
(b) (4) CONFIDENTIAL			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See FCN No. 195, Appendix I

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*

See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
See FCN Nos. 195 and 416.				
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

The dietary exposures to tetrafluoroethylene, (b) (4) and ethoxylated perfluoroether diol are addressed in Section II.G of this form. The safety of the remaining materials potentially present in (b) (4) is as follows. (b) (4) is generally recognized as safe (GRAS) under (b) (4). (b) (4) are direct food substances affirmed as GRAS under (b) (4) respectively. (b) (4) will not be present in the paper food-contact article as it is expected to fully evaporate from the finished paper upon heated drying.

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☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
See FCN Nos. 195 and 416.	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS.

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

See FCN Nos. 195 and 416. GPC data for the perfluoroether diol may be found in Appendix II of FCN No. 195. (b) (4) [redacted]

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☒ Single Use ☒ Repeat Use

(b) (4) [redacted] is intended for use at a level of up to 1.5% by weight as an oil and water repellant in paper and paperboard in contact with all types of food under Condition of Use J, as set forth on FDA's website, at: *www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/ucm109358.htm*, Table 2. Fluorolink® F10 is added prior to sheet formation, or at the size press by weight of dry finished paper or paperboard. Suggested language for describing the FCS, and the applicable limitations for its use in contact with food are given in Appendix V to this submission.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE
(b) (4) [redacted] at a level not to exceed 1.5 weight percent in dry finished paper or paperboard as an oil and water repellant	Food Types I-IX	Condition of Use J

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

See FCN Nos. 195 and 416.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

   No degradation products are expected at Condition of Use J cooking temperatures (350°C for conventional ovens, 130 °C for microwave ovens). *See* thermogravimetric analysis (TGA) curve in Appendix I.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
STRUCTURE		**STRUCTURE**	
SUBSTANCE NAME	**CAS REG. NO.**	**SUBSTANCE NAME**	**CAS REG. NO.**

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (*e.g.*, density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Migration studies conducted on the FCS were reported in FCN No. 416 and are hereby incorporated by reference. The migration studies involved extracting paper treated with the FCS for 2 hours at 175ºC in Miglyol 812 as a fatty food stimulant and for 4 hours at 100ºC in 3% acetic acid and 15% ethanol, as acidic and aqueous foods simulants, respectively.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

See FCN No. 416.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
See FCN No. 416.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

See FCN No. 416.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe assumptions made in deriving the estimates and show all calculations.

The migration studies that Solvay Solexis conducted for FCN Nos. 195 and 416 involved the extraction of paper treated with the FCS for 2 hours at 175°C in Miglyol 182 for fatty foods and 4 hours at 100°C in 3% acetic acid and 15% ethanol for non-fatty foods. We have included a discussion in Appendix II that explains that the time and temperature conditions used for the extraction studies conducted by Solvay Solexis are severe enough to cover applications described by FDA's Condition of Use J. In consideration of this explanation in Appendix II, we believe that the analytical testing conducted by Solvay Solexis is sufficient to accurately demonstrate the amount of migration of (b) (4) from paper and paperboard when used in contact with food at temperatures equivalent to FDA's Condition of Use J.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

The EDI calculations for (b) (4) [redacted] oligomers are presented in Appendix III. These calculations reply upon the data described in Section F of this FCN.

The dietary exposure to the FCS from its use in applications covered by this FCN are the same as the dietary exposures described in FCN No. 416, covering Conditions of Use B through H and microwave susceptor applications. Therefore, no additional dietary exposure would result from the application covered by this FCN.

The EDI calculations for all other compounds that may be present in the FCS are described in FCN No. 195, Section F, which is incorporated here by reference. The estimated dietary exposure to these impurities was based on residual analyses on the diol precursor in conjunction with a calculation of 100% migration from the finished Fluorolink® F-10 polymer. Thus, the EDI for these materials is not affected by the expanded applications for use covered by this FCN.

☒ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (µg/person/day)	CDC (ppb)
Tetrafluoroethylene	116-14-3	0.0021	0.00021	0.00063	
(b) (4)	(b) (4)	0.018	0.0018	0.0054	
		0.12	0.012	0.036	
(b) (4) oligomers*	(b) (4)	47	4.7	14.1	

*Dietary exposure to ethoxylated perfluoroetherdiol is included in the dietary exposure calculations for the (b) (4) ligomers as this precursor diol was quantitated with the oligomers during analysis of (b) (4) in extracts from treated paper. *See* FCN No. 195.

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: March 26, 2010

From: Division of Food Contact Notifications, HFS-275
Chemistry Team 1
Sharon Elyashiv-Barad, Ph.D.

Subject: **FCN 962:** Keller and Heckman, LLP, on behalf of Solvay Solexis S.p.A. (Solvay). Expanded use of diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene (CAS Reg. No. 200013-65-6), to include conditions of use J. Submission received January 11, 2010.

To: Division of Food Contact Notifications, HFS-275
Regulatory Team 2
Attention: M. Hepp, Ph.D.

FCN 962 was submitted by Keller and Heckman LLP (K&H), on behalf of Solvay Solexis S.p.A. (Solvay), to expand the use of the food contact substance (FCS) identified as diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene (CAS Reg. No. 200013-65-6), to include Condition of Use J.

The FCS is also known as phosphate esters of ethoxylated perfluoroether, prepared by reaction of ethoxylated perfluoroether diol (EPFED, CAS Reg. No. 162492-15-1) with phosphorous pentoxide (CAS Reg. No. 1314-56-3) or pyrophosphoric acid (CAS Reg. No. 2466-09-3)

Background

The FCS is effectively notified for use as a water and oil repellent in the manufacture of paper and paperboard, at a level not to exceed 1.5 weight-percent (wt-%) in paper and paperboard, under conditions of use C through H as a result of Solvay's FCN 195[1] (effective 5-14-02). The FCS is also effectively notified for use in paper and paperboard, at a level not to exceed 1.5 wt-% under conditions of use B through H, and at levels up to 1 wt-% in microwave susceptor applications, as a result of Solvay's FCN 416[2] (effective 7-27-04).

The subject FCN was submitted to expand use of the FCS to a level not to exceed 1.5 wt-% in paper and paperboard under condition of use J.

Chemistry information is contained in FDA Form 3480; in Appendices 1 (thermogravimetric analysis, TGA, curve), 2 (migration calculations), and 3 (exposure calculations); and relies on data previously submitted with FCNs 195 and 416. New chemistry information is contained in Appendices 1-3. The notifier's suggested language is contained in Appendix 5.

[1] Chemistry memorandum for FCN 195 dated February 11, 2002 (D. Folmer to A. Shanklin).
[2] Chemistry memorandum for FCN 416 dated July 14, 2004 (P. Turowski to M. Hepp).

Identity and Manufacture (Sections II.A-II.C, and FCNs 195 and 416)

Information on the identity and manufacture of the FCS, including impurities in the FCS, is incorporated by reference from FCNs 195 and 416, and summarized in Sections II.A-II.C of Form 3480. This information was previously reviewed and accepted.[1,2] The chemistry memorandum for FCN 416 is provided as Attachment 1 to this chemistry memorandum for convenience.

We have no questions on the identity and manufacture of the FCS.

Intended Use and Technical Effect (Section II.D)

The FCS is intended for use as an oil and water repellent in the manufacture of paper and paperboard. The FCS will be added to paper and paperboard, at either the wet-end or at the size press, at a level not to exceed 1.5 % wt.-% in the finished paper and paperboard in contact with all foods under conditions of use J.

In Section II.D.3 of Form 3480, the notifier refers to technical effect information included in FCNs 195 and 416. As described in the February 11, 2002 memorandum on FCN 195, the FCS is intended to impart oil and water repellence to food-contact paper and paperboard. Results from two tests designed to determine oil (the Kit Test, TAPPI method 557) and water repellency (the Cobb60 test, TAPPI method T441) were included. The test results indicate increased oil or water repellence in paper as the use level was increased from 0 to 1.5 wt-% in paper.

We have no questions on the proposed use and technical effect of the FCS.

Stability (Sections II.E and Appendix 1)

In Section II.E, the notifier indicated that no degradation products are expected under the proposed conditions of use. The notifier provided a TGA curve in Appendix 1 supporting their claim.

We have no questions on the stability of the FCS.

Migrant Levels in Food (Section II.F and Appendix 2)

In Section II.F, the notifier briefly discussed the migration studies contained in FCN 416. Our initial review of these studies[2] raised concerns regarding the analytical methodology. Rather than basing migrant levels in food on the information contained in FCN 416, the migration behavior of a related grease-proofing agent (FCN 398[3]) manufactured by the same notifier was used to estimate migration of low molecular weight oligomers (LMWOs) of the FCS. See the memorandum on FCN 416 contained in Attachment 1 to this memorandum.

The subject FCN references the migration studies submitted in FCN 416 and indicated that because of the applicability of the studies, there is no increase in migration and thus, no increase in exposure as a result of the proposed use. However, the migration data in FCN 398 (used in lieu of the data in

[3] Chemistry memorandum for FCN 398 dated March 23, 2010 (K. Paquette to P. Honigfort).

FCN 416) only supports Conditions of Use B through H and are not adequate to support the proposed use. Thus, we revisited the migration studies provided in FCN 416. Upon closer examination, we made the following conclusions regarding the comments listed in the July 14, 2004 chemistry memorandum on FCN 416 (see pp. 6-7):

1) we questioned whether a mass range of 800-1700 Daltons used for the LS-MS method would be adequate for quantification of LMWO of <1000 Daltons. We note that this range was also used in FCN 195, where the weight-average molecular weight (Mw) and number-average molecular weight (Mn) were reported as (b) (4) , respectively, and the LMWO fractions were as follows (D=Daltons): (b) (4)

2) we questioned the peak near (b) (4) in the chromatogram. We note that Figure 3 in Appendix II of FCN 416 contains a chromatogram and mass spectrum of a standard solution of the FCS. Thus, even the standard chromatogram contains a peak near (b) (4)

3) we also questioned the peaks observed in the blank controls near To address this concern, we refer to footnote 11 in the February 11, 2002 chemistry memorandum for FCN 195, which indicated that the notifier previously stated that "..the high migration value for the blank paper is the result of (b) (4) eluting at the same retention time as perfluoroether phosphates".

4) finally, we questioned the use of migration modeling as applied to migration from paper rather than a polymer. Inspection of the chemistry memoranda on FCNs 195 and 416 indicates that the migration results were all reported as <0.5 µg/in^2 under all simulants and times tested.[4] Thus, there is really no need to correct the migration values for a low-temperature phase.

Based on our re-evaluation, we are of the opinion that the migration studies submitted in FCN 416 are adequate to support the notified use in FCN 416 as well as the proposed use in the subject FCN (given the testing in Miglyol at 175°C for 2 h).

We have no questions on the migration studies conducted on the FCS.

Consumer Exposure (Section II.G and Appendix 3)

The notifier indicated that the exposure is not expected to change (from FCN 416) as a result of the proposed use.

To the FCS: FCN 416 (Conditions of Use B through H and microwave susceptor applications)

Using a migration value of 47 µg/kg for non-microwave applications (from <0.5 µg/in^2 and 10 g/in^2) and a consumption factor (CF) of 0.1 for uncoated and clay-coated paper, the notifier calculated a dietary concentration (DC) for non-microwave susceptor use of 4.7 ppb. In FCN 416,

[4] FCN 195- 100°C/2h with 10% ethanol, 50% ethanol, n-heptane; FCN 416- 100°C/4 h with 3% acetic acid and 15% ethanol, 175°C/2 h with Miglyol, 6 minutes at 600W microwave with Miglyol.

the exposure to the FCS was refined by using a more realistic CF of 0.05 for paper and paperboard containing grease-proofing agents. Using this refined CF, we now calculate a DC of 2.4 ppb.

Using a migration value of 26 µg/kg (from <0.5 µg/in^2 and 5 g/in^2) and a CF of 0.001 for microwave susceptor applications, we calculate a DC for microwave susceptor use of 0.026 ppb

The total DC is 2.4 ppb + 0.026 ppb or 2.4 ppb

This is significantly lower than what was reported in FCN 416 (9 ppb). This is, in effect, also the revised DC for FCN 416.

To the FCS: FCN 962 (Condition of Use J)

Using a migration value of 47 µg/kg for high temperature, non-microwave applications and a CF of 0.1 for uncoated and clay-coated paper, the notifier calculated a DC of 4.7 ppb. As above, we calculate a DC of 2.4 ppb using a CF of 0.05.

In our April 4, 2006 memorandum on [redacted] (b)(4) we concluded "….that a CF of 0.05 should continue to be used to calculate exposure to grease-proofing agents (and their impurities) intended to contact all food types under Conditions of Use B through H." Although we did not explicitly state that Condition of Use J was included in this analysis, we nonetheless believe that a CF of 0.05 would also be adequate for condition of use J. Given that the migration values were non-detect for all analyses, the CDC would also be 2.4 ppb.[6]

We note that although the migration studies were carried out at 175°C for 2 h, be believe that this temperature would be high enough to encompass all applications of a grease proofing agents on paper and paperboard under Condition of Use J.

To Impurities

The July 14, 2004 chemistry memorandum for FCN 416 indicated that migration values for residual impurities were calculated in FCN 195 using residue levels and assuming 100% migration to food. Since the maximum use level of the FCS remains unchanged, there is no need to modify the migration levels. Our exposure estimates for impurities, summarized below, are identical to FCN 416 and lower than those calculated in FCN 195 since we used a more realistic CF of 0.05 for paper and paperboard containing grease-proofing agents.

[5] Chemistry memorandum for PNC 446 dated April 4, 2006 (K. Paquette to P. Honigfort).

[6] This conclusion would not be applicable if the migration under Conditions of Use B through H and J were different. For example, a higher migration to Miglyol (175ºC/2 h), such as 50 µg/in^2 rather than <0.5 µg/in^2, would necessitate the need to fractionate the CF of 0.05.

Table 1: Summary of exposure estimates for impurities (as taken from FCN 416)

Compound	CAS Reg. No.	DC (µg/kg (ppb))	EDI (µg/p/d)
EPFED	162492-15-1	1	3
TFE	116-14-3	Essentially Zero	Essentially Zero
(b) (4) [redacted]		12	35
		0.0009	0.003
		0.006	0.02

As noted in our February 11, 2002 memorandum on FCN 195, the exposure estimates for impurities were deemed to be conservative. Actual exposure values are likely less that the estimates shown in Table 1.

Cumulative Exposure

The current use of the FCS subsumes the use in FCNs 195 and 416. Therefore, the new cumulative DC, CDC, is 2.4 ppb. We note that this new CDC is lower than the DC initially calculated in FCNs 416 (9 ppb) and 195 (3.7), and the DC reported by the notifier (4.7 ppb).

We have no questions on consumer exposure to the FCS and impurities in the FCS.

Acknowledgment Letter

The acknowledgment letter, as signed off by chemistry on February 3, 2010, includes language that subsumes the uses in FCNs 195 and 416. As discussed at the phase I meeting, we recommend that the listing of FCN 195 on the FDA website indicate that it has been replaced by FCN 416. Second, when the subject FCN becomes effective, we recommend that the listing of FCN 416 indicate that it has been replaced by the subject FCN. Alternatively, the notification language can be modified to indicate that the FCS is intended for use under Condition of Use J.

Summary

We have no further questions on this notification.

Sharon Elyashiv-Barad, Ph.D.

HFS-245 (Begley); CSO; Chemistry Reading File
HFS-275:SElyashiv-Barad:301-436-1169:seb: 3-26-10 (FCN962_C_memo.doc)
RDInit: ABBailey, 03-25-10
Final: seb: 03-26-10

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Compound	CAS Reg. No.	DC (µg/kg (ppb))	EDI (µg/p/d)
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TFE	116-14-3	Essentially Zero	Essentially Zero
(b)(4) [redacted]		12	35
[redacted]		0.0009	0.003
[redacted]		0.006	0.02

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We have no questions on consumer exposure to the FCS and impurities in the FCS.

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The acknowledgment letter, as signed off by chemistry on February 3, 2010, includes language that subsumes the uses in FCNs 195 and 416. As discussed at the phase I meeting, we recommend that the listing of FCN 195 on the FDA website indicate that it has been replaced by FCN 416. Second, when the subject FCN becomes effective, we recommend that the listing of FCN 416 indicate that it has been replaced by the subject FCN. Alternatively, the notification language can be modified to indicate that the FCS is intended for use under Condition of Use J.

Summary

We have no further questions on this notification.

(b)(4) [redacted]

Sharon Elyashiv-Barad, Ph.D.

HFS-245 (Begley); CSO; Chemistry Reading File
HFS-275:SElyashiv-Barad:301-436-1169:seb: 3-26-10 (FCN962_C_memo.doc)
RDInit: ABBailey, 03-25-10
Final: seb: 03-26-10

Attachment 1 to the Chemistry Memorandum for FCN 962:
Chemistry Memorandum for FCN 416

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: July 14, 2004

From: Division of Food Contact Notifications, Chemistry Group I, HFS-275

Subject: FCN 416: Solvay-Solexis S.p.A. via Keller & Heckman; submissions of 3/29/04 and 6/1/04. Phosphate esters of ethoxylated perfluoroether as a water and oil repellent for paper and paperboard.

To: Division of Food Contact Notifications, Regulatory Group I
Attn.: M. Hepp, Ph.D.

Solvay Solexis S.p.A. (Solvay), through their agent Keller and Heckman LLP (K&H), submitted this notification for the use of the food contact substance (FCS) identified as phosphate esters of ethoxylated perfluoroether, prepared by reaction of ethoxylated perfluoroether diol (EPFED) with phosphorous pentoxide or pyrophosphoric acid, for use as a water and oil repellent in the manufacture of paper and paperboard. The FCS is for use at a level not to exceed 1.5 wt-% under conditions of use B-H and at levels up to 1 wt-% in microwave susceptor applications.

The FCS is effectively notified for use at a level not to exceed 1.5 wt-% in paper and paperboard under conditions of use C-H as a result of FCN 195 (Solvay). Information in FCN 195 is incorporated by reference. The FCS and use are similar to those described in FCN 398 (Solvay).

The only new information in this FCN are migration studies (Appendices 1 and 2) and calculations pertaining to migration to food (Appendix 3). Information on the identity, manufacture, chemical/physical specifications and technical effect (Form 3480, Parts II.A-C) was reviewed in the chemistry review memorandum on FCN 195.[7]

As described below, the dietary concentration (DC) for oligomers of the FCS is 9 ppb, and the estimated daily intake (EDI) is 27 µg/p/d.

Identity

Information on the identity of the FCS is summarized in Part II, Sections A and C, of Form 3480 and is consistent with that given in the 2/11/02 memorandum on FCN 195 and summarized below.

7 D. Folmer to A. Shanklin, Memorandum on FCN 195 dated 2/11/02.

Name: Phosphate esters of ethoxylated perfluoroether diol

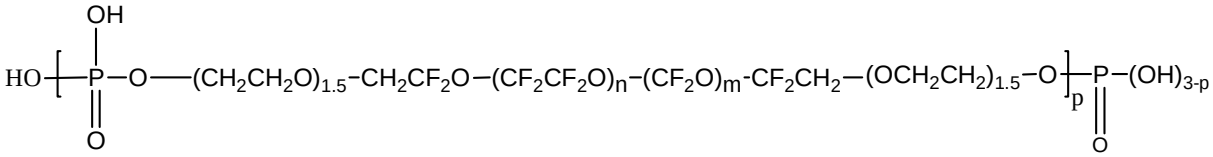
CAS Reg. No.: 200013-65-6

CAS Name: Diphosphoric acid, polymers with ethoxylated reduced methyl esters of reduced polymerized oxidized tetrafluoroethylene

Trade Name: (b) (4)

Molecular weight (for oxidized precursor EPFED): (b) (4)

Structure:



-where (b) for the monoester, and (b) for the diester (b) (4)
-values for n and m are approximately 6

Fluorolink F10 Properties

Table 1. Summary of Physical and Chemical Properties.

Property	**Value**
Functional groups	(b) (4)
Color	
Appearance	
Specific gravity (20º C)	
Dynamic viscosity (20º C)	
Solubility at 25º C	
Water	
(b) (4)	

Characterization. Spectral data identifying the FCS is included in Appendix II of FCN 195. The notifier included an infrared (IR) spectrum of (b) (4) as well as a gel permeation chromatogram (GPC) for EPFED, a precursor of the FCS. The peak at about (b) (4) in the IR spectrum may be attributed to the stretching of the P-O double bond (P=O). The data are consistent with the molecular structure given, and adequately characterize the FCS.

We continue to have no questions on the identity of the FCS.

Manufacture

In Section II.B of Form 3480, the notifier refers to manufacturing and impurity information included in FCN 195, specifically in Appendix I (description of manufacturing process) and Appendix III (information on starting materials and precursors). As described in the 2/11/02 memorandum on FCN 195 and summarized below, the FCS is manufactured (b) (4)
(b) (4)

(b) (4)

(b) (4)

(b) (4)

Impurities. Residue levels for TFE, (see Appendix IV of FCN 195) were determined by analysis of the polymer precursor, EPFED (see II), not the FCS. were extracted using dimethylacetamide followed by analysis using gas chromatography-mass spectrometry (GC-MS). TFE was analyzed by means of head space analysis and gas chromatography employing a flame ionization detector (GC-FID).

Table 2. Impurity Composition

Impurity	CAS #	Residual Level
EPFED	162492-15-1	(b) (4)
(b) (4)		< 0.3 wt-%
		< 1 wt-%
		< 0.1 wt-%
		< 0.2 wt-%
Tetrafluoroethylene (TFE)	116-14-3	(b) (4)
Ethylene oxide (EO)	75-21-8	< 240 ppb (residual level in precursor)
1,4-dioxane	123-91-1	< 1.6 ppm (residual level in precursor)

(b) (4) claimed by the notifier to be generally recognized as safe (GRAS) under (b) (4). The notifier claims that (b) (4) would not be present in the FCS since all (b) (4) (b) (4)

We have no questions on the manufacture and impurities of the FCS. We have two additional comments since review of the chemistry information in FCN 195.

Potential for . It is our judgment that (b) (4) (b) (4) We agree that the likelihood of the formation of (b) (4)

(b) (4) (b) (4)

Low Molecular Weight Oligomers. In Section II.C.2 of Form 3480, the notifier states that the molecular weight distribution (MWD) of the FCS is expected to be similar to that of EPFED. A GPC of EPFED (Appendix II of FCN 195, also see the 12/18/01 submission to FCN 195) demonstrated that the percentage of oligomers as a function of molecular weight is as follows: ≤800 Daltons, 1.7%; ≤980 Daltons, 3.8%; ≤1030 Daltons, 5.1%. We thus will assume that the FCS contains at most 5% low molecular weight oligomers (LMWO).

Use, Use Level, and Intended Technical Effect

In Section II.D of Form 3480, the notifier states that the FCS is intended as an oil and water repellant in the manufacture of food-contact paper and paperboard. The FCS will be added to paper and paperboard, at either the wet-end or at the size press, at a level not to exceed 1.5% by weight in the finished paper and paperboard. Paper containing the FCS at a level not to exceed:

1) 1.5% by weight of the finished paper and paperboard will be used in contact with all food types under Conditions of Use B-H. *This FCN would include condition of use B to the notified use in FCN 195.*
2) 1% by weight of the finished paper and paperboard, will be used in contact with all food types in microwave susceptor applications.

Draft language for the notification letters is contained in Appendix 5 of the FCN. Given that the proposed use subsumes that in FCN 195, the notifier may wish to withdraw FCN 195.

In Section II.D.3 of Form 3480, the notifier refers to intended technical effect information included in FCN 195. As described in the 2/11/02 memorandum on FCN 195, the FCS is intended to impart oil and water repellence to food-contact paper and paperboard. Results from two tests designed to determine oil (the Kit Test, TAPPI method 557) and water repellency (the Cobb60 test, TAPPI method T441) are included. The test results indicate increased oil or water repellence in paper as the use level was increased from 0 to 1.5 wt-% in paper.

We have no questions on the proposed use and intended technical effect of the FCS.

Migration Levels in Food

Migration studies conducted on paper samples manufactured with the FCS are summarized in Section II.F of Form 3480. The full studies are contained in Appendices 1 and 2 to the FCN. Appendix 1 contains a migration study involving conventional heating while Appendix 2 contains a migration study using microwave susceptors. Both studies were conducted by TNO Nutrition and Food Research Institute. As described in detail under Comments, we have not used the results of these studies to estimate consumer exposure.

Conventional heating. Two types of paper samples were treated with 1.5 wt.-% of the FCS, one by slurry addition (TNO code (b) (4)) and another by size press addition (TNO code (b) (4) The paper samples were tested using 3% acetic acid and 15% ethanol (non-fatty simulant) at 100ºC for 4 h and Miglyol 812 (fatty simulant) at 175ºC for 2 h. Appendix 3 of the

FCN contains calculations using diffusion principles to demonstrate that the testing conditions, which had no low temperature phase, were nonetheless acceptable to model condition of use B (100ºC/2 h, 40ºC/ 238 h). We agree with this conclusion, although, as discussed in the Estimation of Oligomer Migration section, we do not accept the notifier's method.

Test paper samples (10 cm x 15 cm) were cut into small pieces (1 cm x 3 cm) and placed in a headspace vial (50 pieces, 23 in^2 1-sided), food simulant added (40 mL), the vial closed and heated in an oven at 100ºC for 4 h (non-fatty) and 175º C for 2 h (fatty). The sample mass-to-surface area ratio was about 2 mL/in^2, an acceptable value for migration studies conducted on paper samples. At the end of each time period, the aqueous extracts were evaporated to dryness and the residues dissolved in isopropanol (1 mL), while the Miglyol extracts were extracted into a methanol-ammonia solution, evaporated to dryness, and the residues dissolved in isopropanol (1 mL). The isopropanol extracts were analyzed by high performance liquid chromatography with mass spectrometric detection (LC-MS) in the range of m/z 800-1700. The LS-MS method is described in the appendix to the TNO report. All testing was conducted in triplicate. Controls (blanks) consisted of simulants treated as above with no test samples.

A calibration curve was prepared from sequential dilution of a stock solution of the FCS in isopropanol (7.3278 mg/mL) to give standards containing 0, 10.99, 14.66, 18.32, 21.98, 25.65, 29.31, 32.48, 36.64, 43.97, 51.29, 58.62, 65.95 and 73.128 µg/mL. The calibration curve and supporting data are shown in Figures 11-12 of the TNO report. The calibration curve was constructed by summing the peak areas of all the peaks in the m/z 800-1700 range. A representative spectrum for a calibration standard is shown in Figure 10 of Appendix 1.

The FCS was not detected in any of the extracts at a reported limit of detection (LOD) of <7.3 $µg/dm^2$ (<0.5 $µg/in^2$). Using the volume of extract for LC-MS (1 mL) and the surface area (23 in^2), this corresponds to 11 µg/mL. This is actually the lowest standard concentration. Inspection of Figure 10 in the TNO study indicates that an actual LOD would be expected to be much lower. Validation studies were conducted by spiking the extracts at about 15 µg/mL which is slightly higher than the reported LOD. The recoveries were acceptable. Blank, standard, test sample and validation LC-MS results are contained in the TNO study.

Microwave heating. The test sample (TNO code (b) (4) consisted of two layers of paper, manufactured with 1 wt.-% of the FCS, each bound to a metallized plastic film with an acrylic adhesive. Paper samples (18 cm x 12 cm) were folded into shallow trays and filled with Miglyol 812 (43 g, height of 0.6 cm, surface area of 21 in^2). This corresponds to a volume-to-surface area of about 2 mL/in^2. (The notifier used a 2-sided surface area rather than 1-sided). The contents were heated in a 600W microwave oven for 6 minutes. A beaker with water (90 mL) was used as an inert load.

At the end of each time period, the extracts were treated as described above, that is extraction into an ammoniacal methanol-water mixture, dissolved in IPA (1 mL) and analyzed by LC-MS. The FCS was not detected at an LOD of 11 µg/mL, corresponding to 0.5 $µg/in^2$. Validation studies were conducted as described above and the recoveries were acceptable. Blank, standard, test sample and validation LC-MS results are contained in the TNO study.

Comments. We have the following comments on the migration studies:

First, the mass range used for quantification in the LS-MS method for the subject FCN and FCN 195 was m/z 800-1700. We are concerned that this range would not be useful in quantification of LMWO of <1000 Daltons that are expected to be the primary migrants. To illustrate this concern by way of an example, consider Figure 3 in Appendix 1. Figure 3 is the chromatogram and mass spectrum obtained from analysis of the 3% acetic acid extract from the paper sample with the FCS added to the pulp slurry. Inspection of the chromatogram indicates a peak near (b) (4) with a noisy baseline. The accompanying mass spectrum is also noisy and does not contain any information on quantification below 900 Daltons, the mass range at which any LMWO migrants would be expected to appear.

Furthermore, we have no information that confirms that the LC peak near (b) (4) used to quantify migration is suitable for detection of LMWO migrants. The notifier did not provide LC/MS data for a sample containing concentrated LMWO.

Also of concern is the fact that some of the blank controls have peaks in the LC region of interest (b) (4). Inspection of the chromatograph of the blank in Figure 2 (Appendix 1) suggests the presence of some material in the blank that would interfere with detection of the FCS. No rationale for this observation of several peaks at the retention time of interest (b) (4) was contained in the TNO report. Similar peaks near (b) (4) were also observed in chromatograms of blank controls in FCN 195 (Appendix IV, figs. 7, 12, 13, 16, 17, etc.)

Estimation of Oligomer Migration. Because of our concerns with the analytical method used in the migration studies, we considered alternate methods to quantify oligomer migration. In Appendix 3, the notifier estimated diffusion coefficients for a representative oligomer (500 Da) of the FCS to demonstrate that the migration protocols used to simulate conventional heating were equivalent to or more severe than those we recommend for Conditions of Use B. However, these diffusion coefficients (2×10^{-13} cm^2/s @40°C, 5×10^{-11} cm^2/s @100°C, 5×10^{-9} cm^2/s @175°C) cannot be used to model migration of the FCS from paper because they were calculated assuming Fickian diffusion through a polymeric substrate, not paper. The calculations further assumed a diffusivity constant ($A_p = 0$) which is average for polymers but presumably quite low for paper. According to Tim Begley of the Indirect Additives Group in FDA's Division of Chemistry Research and Environmental Review, a few diffusion coefficients for paper that have been estimated were approximately 10^{-9} for "normal" temperatures.

Migration of Perfluoropolyether Oligomers from FCN 398. Rather than basing migration levels in food on the submitted migration studies or modeling, we believe that the migration behavior of a related grease-proofing agent manufactured by the same notifier can be used to estimate migration of LMWO of the FCS. The related grease-proofing agent is the subject of FCN 398, perfluoropolyether dicarboxylic acid ammonium salt (b) (4) We believe that the migration behavior of (b) (4) may be used to estimate migration for the subject FCS for the following reasons:

1. (b) (4) is expected to have similar perfluoropolyethylether oligomers as the FCS, (b) (4) Both Fluorolink compounds have the same polymer repeat unit $(CF_2\text{-}CF_2\text{-}O\text{-})_n$, albeit different end groups.

2. (b) (4) has a MW that is similar to that of the FCS ((b) (4)) while the percentage of LMWO (22 wt-%) is more than quadruple that in the FCS (<5 wt-%).

3. The ammonium carboxylate end units of (b) (4) would ensure good solubility in aqueous solvents, similar to the phosphate ester end groups of the FCS. In fact, (b) (4) may well migrate more readily from paper than the FCS, whose phosphate ester groups may be more tightly bound to the paper than carboxylate groups.

4. Migration testing of paper containing 1% (b) (4) into water, 3% acetic acid, and isooctane was conducted under condition of use B and analyzed by LC-MS using the full mass range of 120-2000 Da. LMWO were clearly detected under these conditions for the $C10/NH_4$ standards and blank controls after standard addition (see FCN 398 Appendix 7, Figs 7, 10, 13, 16-20).

Migration tests in food simulants under migration protocol B on paper treated with 1 wt-% (b) (4) were reported as follows (as taken from Table I in our 3/23/04 memorandum on FCN 398):

Table 3. Migration Values for Perfluoropolyether Oligomers from (b) (4)

Food Simulant	**Water**	**3% Acetic Acid**	**Isooctane**
Concentration in Food (mg/kg)[a]	0.14	< 0.02	< 0.02

[a]Assuming 10 g of food contact 1 in^2 of packaging material.

Although the use level of the FCS is 1.5 wt-%, whereas that of (b) (4) is 1 wt-%, we nonetheless consider the migration values reproduced in Table 3 to be a conservative estimate of the migration of the FCS under conditions of use B-H.

As described in our 3/23/04 memorandum on FCN 398, migration calculations were used to estimate migration of Fluorolink $C10/NH_4$ into alcoholic food, since an alcoholic food simulant was not used in the migration tests. In a similar manner, we estimated migration of oligomers of the subject FCS assuming all of the available oligomers of MW < 1000 (5 wt-% of the FCS) migrate to alcoholic foods. The calculation, which is based on a maximum concentration of 1.5 wt-% FCS in the finished paper, an average paper basis weight of 0.052 g/in^2, and our usual assumption that 10 g of food contact 1 in^2 of packaging material, follows:

$$\frac{0.05 \text{ g oligomers}}{\text{g FCS}} \left| \frac{0.015 \text{ g FCS}}{\text{g paper}} \right| \frac{0.052 \text{ g paper}}{in^2} \left| \frac{in^2}{10 \text{ g food}} \right. = 3.9 \text{ mg/kg oligomers in food}$$

Oligomer Migration under Microwave Susceptor Conditions. We used a similar calculation assuming 100% migration of LMWO, to estimate migration of oligomers from use of the FCS in microwave suspectors. Using a maximum concentration of 1.0 wt-% FCS in microwave susceptor

paper, we obtained a conservative migration value of 2.6 mg/kg oligomers in food.

Consumer Exposure

The notifier's exposure estimates for the FCS are summarized in Section II.G of Form 3480. Exposure to oligomers is discussed in Appendix 4 of the FCN. The notifier determined an oligomers dietary concentration (DC) of 4.7 ppb. We will not comment on the notifier's values.

Oligomers of the FCS. We determined a DC of 9 ppb (9 µg/kg) as follows based on the migration values discussed above.

Migration values of 140 µg/kg, 20 µg/kg, 20 µg/kg, and 3900 µg/kg were used to model migration into aqueous, acidic, fatty, and low alcohol foods, respectively, for use of the FCS under conditions of use B-H. Using a consumption factor (CF) of 0.05 for paper/ paperboard treated with grease-proofing agents and the food-type distribution factors (f_t) for the uncoated paper packaging category (f_{aq} = 0.57, f_{ac} = 0.01, f_{fat} = 0.41, f_{al} = 0.01), the DC of FCS oligomers under use B-H is:

$$DC = 0.05\ CF\ [(0.57\ f_{aq})(140\ \mu g/kg) + (0.01\ f_{ac})(20\ \mu g/kg) + (0.01\ f_{al})(3900\ \mu g/kg) + + (0.41\ f_{fat})(20\ \mu g/kg)] = 6.4\ ppb$$

Using the migration value of 2.6 mg/kg and a CF of 0.001 for microwave susceptor applications, the DC for microwave susceptor use is (the 100% migration estimate into alcoholic food was included in the DC above):

$$DC = 0.001\ CF\ [(0.99\ f_{aq} + f_{ac} + f_{fat})(2600\ \mu g/kg)] = 2.6\ ppb$$

The combined DC of oligomers is 6.4 ppb + 2.6 ppb = 9 ppb (9 µg/kg).

Assuming a daily diet of 3000 grams of food/p/d, the estimated daily intake (EDI) of the FCS oligomers is 27 µg/p/d.

Impurities. As stated by the notifier, migration values of residual impurities were calculated in FCN 195 under a 100% migration model. The maximum use level of the FCS remains unchanged so modification of migration levels was not necessary. Our exposure estimates for impurities, summarized in Table 4, are lower than those calculated in FCN 195. We used a more realistic CF of 0.05 for paper/paperboard containing grease-proofing agents.

Table 4. Summary of exposure estimates.

Compound	CAS Reg. No.	DC (µg/kg (ppb))	EDI (µg/p/d)
Oligomers of the FCS	(200013-65-6)	9	27
EPFED	162492-15-1	1	3
(b) (4)		12	35
TFE	116-14-3	Essentially Zero	Essentially Zero
(b) (4)		0.0009	0.003
		0.006	0.02

Cumulative Exposure
The current use of the FCS subsumes that in FCN 195, such that the cumulative DC and EDI (CDC and CEDI) are 9 ppb and 27 µg/p/d, respectively.

Notification Language

The language used in the acknowledgement letter dated 6/29/04 is appropriate. Given that the proposed use subsumes that in FCN 195, the notifier may wish to withdraw FCN 195.

Conclusions

The exposure calculations for oligomers of the FCS led to the determination of a dietary concentration of **9 µg/kg** (or 9 ppb) which corresponds to an EDI of **27 µg/p/d**. This is also the CEDI.

We have no questions.

Petra Turowski, Ph.D.

HFS-205 (Kuznesof); 245 (Begley); Chemistry Reading File
HFS-275:PTurowski:418-0508:FCN0416_c_memo.doc:Pt:6/28/04
Init:ABailey:7/14/04
Final:Pt:7/14/04

CHEMOURS FCN 510

FOR USE IN REPEATE-USE
FOOD CONTACT ARTICLES

FDA CHEMISTRY MEMO IS
INCOMPLETE

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Copolymer of 1,1-difluoroethylene (CASRN 75-38-7), hexafluoropropene (CASRN 116-15-4), and tetrafluoroethylene (CASRN 116-14-3)

2. CAS Registry Number

As indicated above

3. Trade or Common Name

4. Other Chemical Names (IUPAC, etc.)

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5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a fluoroelastomer manufactured from the following monomers: 1,1-difluoroethylene (VF2), hexafluoropropene (HFP), and tetrafluoroethylene (TFE). The following are compositions of representative polymer products Viton® GF-200S and Viton® GBL-200S:

Monomer	CAS Reg. No.	Viton® GF-200S Weight - %	Viton® GBL-200S Weight - %
VF2	75-38-7	(b	
HFP	116-15-4	(b	
TFE	116-14-3	(b	

The molecular formula for the polymer is $(CH_2=CF_2)_a - (CF_3CF=CF_2)_b - (CF_2=CF_2)_c$

GPC analysis of the representative samples of the FCS yielded the following results:

M_n = (b) (4) Daltons (Viton® GF-200S), (b) (4) Daltons (Viton® GBL-200S); M_w = (b) (4) Daltons (Viton® GF-200S), (b) (4) Daltons (Viton® GBL-200S) (*See* **Attachment 1** for results of GPC analyses for the FCS).

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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See **Attachment 2** for infrared spectra for the FCS.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
1,1-Difluoroethylene (VF2)	75-38-7	Starting monomer
Hexafluoropropene (HFP)	116-15-4	Starting monomer
Tetrafluoroethylene (TFE)	116-14-3	Starting monomer
(b) (4)		Cure site monomer
		Chain transfer agent
		Surfactant
		Polymerization medium
Barium sulfate	7727-43-7	Surface treatment/partitioning agent
(b) (4)		Dispersion destabilizer
		Buffer
		Initiator

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 3** for a description of the manufacturing process for two grades of the FCS.

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Section B - MANUFACTURE - Continued

9. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
TFE	116-14-3	-	ND (1.9 ppm LOD)
VF2	75-38-7	-	ND (68.4 ppb LOD)
HFP CONFIDENTIAL	116-15-4	-	ND (160.2 ppb LOD)
(b) (4)		-	ND (7.5 ppm LOD)
See **Attachment 4** for results of residual monomer testing for the FCS.			

Ensure that exposures to these substances are addressed in Section II.G of this form.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications.

Property	Max. Value	Min. Value	Individual Batch Values
See **Attachment 5** for information concerning the polymer properties and specification test results of three batches of the FCS.			

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

[redacted]. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

GPC analyses of the FCS indicates that the maximum percentage of oligomeric species below 1000 Daltons is less than 0.01%. *See* **Attachment 1** for results of GPC analyses for the FCS.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

Intended Use: In the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment, under all use conditions in contact with all types of food.

Specifications/Limitations: The base fluoropolymer may be compounded with no more than 3.0 parts per hundred of rubber (phr) of trially isocyanurate and no more than 2.5 phr of 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane. Rubber articles containing the FCS used in contact with aqueous food shall meet the total extractive limitations prescribed in 21 CFR 177.2600(e) and rubber articles containing the FCS used in contact with fatty food shall meet the total extractive limitations prescribed in 21 CFR 177.2600 (f).

A recommended description of the notification for use in FDA's public inventory is provided in **Attachment 6**.

[redacted] a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

[redacted]

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Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS is intended to be used as a component of repeated use food-contact articles, primarily molded parts for food processing equipment, such as o-rings, gaskets, diaphragms, and other materials, that function primarily in sealing applications. A representative use in contact with food is in a food processing line as part of o-ring seal applications. In such an application, a maximum of 1500 seals, each with a food-contact area of 0.496 in^2, would be used on a given piece of equipment to process 4,320,000 gallons of food. The total surface area of 1500 seals each with a food-contact area of 0.496 in^2 is (1500 seals) x (0.496 in^2/seal) = 744 in^2. A volume of 4,320,000 gallons is equivalent to (4.32 x 10^6 gallons) x (3785 mL/gallon) = 1.64 x 10^{10} mL. Assuming a density of 1 g/cm^3 for the food, this corresponds to 1.64 x 10^{10} grams of food. Thus, a representative food mass-to-surface area ratio is (1.64 x 10^{10} grams) ÷ (744 in^2) = 2.2 x 10^7 g/in^2.

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. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

The FCS is a material that will be used as the basic polymer for the manufacture of molded rubber parts for food processing equipment.

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None.

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2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Two representative grades of the FCS were tested, Viton® GF-200S and Viton® GBL-200S, having the following polymeric composition:

Monomer	Level, Viton® GF-200S	Level, Viton® GBL-200S
TFE	CONFIDENTIAL (b) (4)	CONFIDENTIAL
VF2		
HFP		

The test samples were cured using triallyl isocyanurate and 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and contained 100 parts polymer, 2.5 parts triallyl isocyanurate, 2.5 parts 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and 3.0 parts zinc oxide. Each sample had a thickness of 0.075 inches (75 mils) and a surface area of 43.8 in^2, and were extracted by total immersion. There are no detectable levels of any of the monomers in these polymers; detection limits for the monomers are discussed in Section II-F-2 below.

Reports of extraction studies performed on these two grades of the FCS are appended as **Attachment 7**. In these reports, the Viton® GF-200S sample was identified as Compound 1770A08-01 and the Viton® GBL-200S sample was identified as Compound 1770A08-02.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

The test samples were extracted with water and hexane in a Soxhlet extractor, each solvent at its boiling point. The test samples were exposed to boiling water or boiling hexane for 7 hours, followed by a fresh aliquot of either boiling water or hexane for an additional 2 hours.

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Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in² 0.011 mg/in² 0.021 mg/in²	0.015 mg/in²
			40°C analysis after 24 hours	0.015 mg/in² 0.014 mg/in² 0.022 mg/in²	0.017 mg/in²
			40°C analysis after 96 hours	0.017 mg/in² 0.017 mg/in² 0.023 mg/in²	0.019 mg/in²
			40°C analysis after 240 hours	0.020 mg/in² 0.021 mg/in² 0.023 mg/in²	0.021 mg/in²

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Viton® GF-200S	Total non-volatiles	Water	Boiling/7 hours	0.0 mg/in^2	-
	Total non-volatiles	Water	Boiling/additional 2 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/7 hours	0.390 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/additional 2 hours	0.0 mg/in^2	-
Viton® GBL-200S	Total non-volatiles	Water	Boiling/7 hours	0.0 mg/in^2	-
	Total non-volatiles	Water	Boiling/additional 2 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/7 hours	0.005 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/additional 2 hours	0.0 mg/in^2	-

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Section F - MIGRATION LEVELS IN FOOD - Continued

2. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

See **Attachment 8**.

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Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Not applicable.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

See **Attachment 9**.

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Table 5: Exposure estimates			
Substance	**Use level (%)**	**DC (ng/kg or pptr)**	**EDI (ng/p/d)**
FCS (as LMWOs)		8.6	26
VF2		Essentially zero	
HFP		Essentially zero	
TFE		Essentially zero	
(b) (4)	0.26	2.6	7.8
	0.52	5.3	15.9
		Essentially zero	
Barium sulfate	1.0	10	30
(b) (4)		GRAS (b) (4)	
		GRAS	
		Essentially zero	
TAIC	3.0	31	93
tert-Butyl alcohol	1.3*	13	39
2,5-dimethylhexane-2,5-diol	1.3*	13	39
Zinc oxide		GRAS 182.8991	
(b) (4)		GRAS (b) (4)	

* The "use level" for these substances was calculated by determining the number of moles of each compound generated from the initiator DBPH and multiplying this number by their respective molecular weights.

We have no questions on consumer exposure for the FCS or impurities in the FCS.

Notification Language

The acknowledgment letter, as signed off by Chemistry on June 24, 2005, is appropriate as written.

Conclusion

We have no questions on this FCN.

(b) (6)

Sharon Elyashiv-Barad, Ph.D.

HFS-275 (Cheeseman); HFS-245 (Begley); Chemistry Reading File
HFS-275:SElyashiv-Barad:436-1169:seb:9-2-05 (FCN510_C_memo)
RDInit: ABBailey, 8-30-05
Final: seb, 9-2-05

CHEMOURS FCN 511

FOR USE IN REPEATE-USE
FOOD CONTACT ARTICLES

FDA CHEMISTRY MEMO IS
INCOMPLETE

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Copolymer of 1,1,-difluoroethylene (CASRN 75-38-7), tetrafluoroethylene (CASRN 116-14-3), and trifluoromethyl trifluorovinyl ether (CASRN 1187-93-5)

2. CAS Registry Number

As indicated above

3. Trade or Common Name

4. Other Chemical Names (IUPAC, etc.)

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5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a fluoroelastomer manufactured from the following monomers: 1,1-difluoroethylene (VF2), tetrafluoroethylene (TFE), and trifluoromethyl trifluorovinyl ether (PMVE). The following is the composition of a representative polymer product, Viton® GFLT-200S:

Monomer	CAS Reg. No.	Viton® GFLT-200S Weight - %
VF2	75-38-7	(b
TFE	116-14-3	(b
PMVE	1187-93-5	(b

The molecular formula for the polymer is $(CH_2=CF_2)_a - (CF_2=CF_2)_b - ((CF_3O)CF=CF_2)_c$
GPC analysis of the representative samples of the FCS yielded the following results:

M_n = (b) (4) (Viton® GFLT-200S); M_w = (b) (4) Daltons (Viton® GFLT-200S). *See* **Attachment 1** for results of GPC analyses for the FCS.

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6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See **Attachment 2** for infrared spectrum for the FCS.

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
1,1-Difluoroethylene (VF2)	75-38-7	Starting monomer
Trifluoromethyl trifluorovinyl ether (PMVE)	1187-93-5	Starting monomer
Tetrafluoroethylene (TFE)	116-14-3	Starting monomer
(b) (4)		Cure site monomer
		Chain transfer agent
		Surfactant
		Polymerization medium
Barium sulfate	7727-43-7	Surface treatment/partitioning agent
(b) (4)		Dispersion destabilizer
		Buffer
		Initiator

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 3** for a description of the manufacturing process for a representative grade of the FCS.

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Section B - MANUFACTURE - Continued

5. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
TFE	116-14-3	-	ND (2.0 ppm LOD)
VF2	75-38-7	-	ND (70.9 ppb LOD)
PMVE	1187-93-5	-	ND (184.2 ppb LOD)
(b)	(b) (4)	-	ND (7.5 ppm LOD)
See **Attachment 4** for results of residual monomer testing for the FCS.			

Ensure that exposures to these substances are addressed in Section II.G of this form.

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

a. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications. *See* **Attachment 5** for further detail concerning the polymer properties and specification test results of three batches of the FCS.

Property	Max. Value	Min. Value	Individual Batch Values
Volatile loss, wt % at 130°C	(b) (4)		
Mooney viscosity, ML 1+10 at 121°C			
Inherent viscosity			
Wt % Fluorine			
Wt % Vinylidene fluoride			
Wt % Perfluoro (methyl vinyl ether)			
Wt % Tetrafluoroethylene			
Wt % (b) (4)			

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

3. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

GPC analyses of the FCS indicates that the maximum percentage of oligomeric species below 1000 Daltons is less than 0.01%. *See* **Attachment 1** for results of GPC analyses for the FCS.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

Intended Use: In the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment, under all use conditions in contact with all types of food.

Specifications/Limitations: The base fluoropolymer may be compounded with no more than 3.0 parts per hundred of rubber (phr) of trially isocyanurate and no more than 2.5 phr of 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane. Rubber articles containing the FCS used in contact with aqueous food shall meet the total extractive limitations prescribed in 21 CFR 177.2600(e) and rubber articles containing the FCS used in contact with fatty food shall meet the total extractive limitations prescribed in 21 CFR 177.2600 (f).

A recommended description of the notification for use in FDA's public inventory is provided in **Attachment 6**.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

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Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS is intended to be used as a component of repeated use food-contact articles, primarily molded parts for food processing equipment, such as o-rings, gaskets, diaphragms, and other materials, that function primarily in sealing applications. A representative use in contact with food is in a food processing line as part of o-ring seal applications. In such an application, a maximum of 1500 seals, each with a food-contact area of 0.496 in^2, would be used on a given piece of equipment to process 4,320,000 gallons of food. The total surface area of 1500 seals each with a food-contact area of 0.496 in^2 is (1500 seals) x (0.496 in^2/seal) = 744 in^2. A volume of 4,320,000 gallons is equivalent to (4.32×10^6 gallons) x (3785 mL/gallon) = 1.64×10^{10} mL. Assuming a density of 1 g/cm^3 for the food, this corresponds to 1.64×10^{10} grams of food. Thus, a representative food mass-to-surface area ratio is (1.64×10^{10} grams) ÷ (744 in^2) = 2.2×10^7 g/in^2.

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. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

The FCS is a material that will be used as the basic polymer for the manufacture of molded rubber parts for food processing equipment.

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None.

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2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

000011

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

One representative grade of the FCS was tested, Viton® GFLT-200S, having the following polymeric composition:

CONFIDENTIAL

Monomer	Level, Viton® GFLT-200S
VF2	(b)
TFE	(b)
PMVE	(b)

CONFIDENTIAL

The test sample was cured using triallyl isocyanurate and 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and contained 100 parts polymer, 2.5 parts triallyl isocyanurate, 2.5 parts 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and 3.0 parts zinc oxide. Each sample had a thickness of 0.075 inches (75 mils) and a surface area of 43.8 in^2, and were extracted by total immersion. There are no detectable levels of any of the monomers in these polymers; detection limits for the monomers are discussed in Section II-F-2 below.

A report of the extraction study performed on GFLT-200S is appended as **Attachment 7**. In this report, the Viton® GFLT-200S sample is identified as Compound 1770A08-03.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

The test samples were extracted with water and hexane in a Soxhlet extractor, each solvent at its boiling point. The test samples were exposed to boiling water or boiling hexane for 7 hours, followed by a fresh aliquot of either boiling water or hexane for an additional 2 hours.

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Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in^2) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in^2. For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in^2 0.011 mg/in^2 0.021 mg/in^2	0.015 mg/in^2
			40°C analysis after 24 hours	0.015 mg/in^2 0.014 mg/in^2 0.022 mg/in^2	0.017 mg/in^2
			40°C analysis after 96 hours	0.017 mg/in^2 0.017 mg/in^2 0.023 mg/in^2	0.019 mg/in^2
			40°C analysis after 240 hours	0.020 mg/in^2 0.021 mg/in^2 0.023 mg/in^2	0.021 mg/in^2

000013

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Viton® GFLT-200S	Total non-volatiles	Water	Boiling/7 hours	0.0 mg/in^2	-
	Total non-volatiles	Water	Boiling/additional 2 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/7 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/additional 2 hours	0.0 mg/in^2	-

000014

Section F - MIGRATION LEVELS IN FOOD - Continued

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

See **Attachment 8**.

000015

Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Not applicable.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

See **Attachment 9**.

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and gaskets. Therefore, exposure to (b) (4) is expected to be essentially zero.

The notifier also claims that the (b) (4) will be removed during the manufacturing process when (b) (4). We do not agree with the notifier's assumption and have calculated an exposure using the approach used for (b) (4) As reported in the 5/18/05 update, the maximum use level of this mixture is 0.52%. Exposure to either component of this mixture would be no greater than 5.3 pptr. The DCs and EDIs of the FCS and its impurities are summarized in Table 1.

Table 1. Exposure estimates

Substance	Maximum Residual Level	Use level (ppm)	DC (pptr)	EDI (ng/p/d)
Oligomers			5	15
VF2	< 2.0 ppm			Essentially zero
TFE	<70.9 ppb			Essentially zero
PMVE	<184 ppb			Essentially zero
(b) (4)	<7.5 ppm	2400	2.5	7.4
		5200	5.3	16
Barium sulfate		10000	10	30
Triallyl isocyanurate		30000	31	93
tert-Butyl alcohol		13000[a]	13	39
2,5-dimethylhexane-2,5-diol		13000[a]	13	39
Zinc oxide				GRAS 182.8991
(b) (4)				Essentially zero
(b) (4)				GRAS (b) (4)
(b) (4)				Essentially zero
(b) (4)				GRAS (b) (4)
(b) (4)				GRAS (b) (4)

a. The "use level" for these materials was calculated by determining the number of moles of each compound generated from the initiator DBPH and multiplying this number by their respective molecular weights.

Conclusion

The chemistry and exposure data submitted in support of this FCN were evaluated and found to be adequate to support a safety decision.

CHEMOURS FCN 539

FOR USE IN REPEATE-USE
FOOD CONTACT ARTICLES

Part II — CHEMISTRY INFORMATION

Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Copolymer of 4-bromo-3,3,4,4-tetrafluoro-1-butene (CASRN 18599-22-9), ethylene (CASRN 74-85-1), tetrafluoroethylene (CASRN 116-14-3), and trifluoromethyl trifluorovinyl ether (CASRN 1187-93-5)

2. CAS Registry Number

105656-63-1

3. Trade or Common Name

4. Other Chemical Names (IUPAC, etc.)

5. Description

Provide a description of the FCS, including chemical formula(e), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The FCS is a fluoroelastomer manufactured from the following monomers: 4-bromo-3,3,4,4-tetrafluoro-1-butene (BTFB), ethylene, tetrafluoroethylene (TFE), and trifluoromethyl trifluorovinyl ether (PMVE). The following is the composition of a representative polymer product, (b) (4)

Monomer	CAS Reg. No.	(b) (4)
BTFB	18599-22-9	
Ethylene	74-85-1	
TFE	116-14-3	
PMVE	1187-93-5	

The molecular formula for the polymer is (b) (4)

(b) (4)

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See **Attachment** 1 for infrared spectrum for the FCS.

000007

Section B - MANUFACTURE

See Chemistry Recommendations Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, including their chemical names, CAS Registry Numbers, and functions in the manufacture of the FCS.

Chemical Name	CAS Reg. No.	Function
4-Bromo-3,3,4,4-tetrafluoro-1-butene	18599-22-9	Starting monomer
Ethylene	74-85-1	Starting monomer
Trifluoromethyl trifluorovinyl ether (PMVE)	1187-93-5	Starting monomer
Tetrafluoroethylene (TFE)	116-14-3	Starting monomer

(b) (4)

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See **Attachment 2** for a description of the manufacturing process for a representative grade of the FCS.

000008

Section B - MANUFACTURE - Continued

List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations.

Chemical Name	CAS Reg No.	Typical Residual (%)	Maximum Residual (%)
(b) (4)		-	ND (2.57 ppb LOD)
		-	ND (26.5 ppm LOD)
		-	ND (0.52 ppm LOD)
		-	ND (47.7 ppb LOD)

Ensure that exposures to these substances are addressed in Section II.G of this form.

000009

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations Section II.A.5 and 6

1. For non-polymeric FCSs, provide physical/chemical specifications, such as density, melting point, maximum impurity levels, and solubility in food simulants.

Property	Value

2. In addition, provide the following relevant information for polymeric FCSs:

. Polymer Properties and Specification Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide specification test results for at least three production batches of the FCS. Attach methods for establishing compliance with specifications. *See* **Attachment 4** for further detail concerning the polymer properties and specification test results of three batches of the FCS.

Property	Max. Value	Min. Value	Individual Batch Values

(b) (4)

Part II — CHEMISTRY INFORMATION - CONTINUED

Section C - PHYSICAL/CHEMICAL SPECIFICATIONS - Continued

Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons.

Not applicable. As noted above, the FCS is insoluble and, therefore, it is not possible to perform GPC analyses for molecular weight information for the polymer.

Section D - INTENDED USE

See Chemistry Recommendations Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. State whether single or repeated use is intended.

Intended Use: For repeat-use in the fabrication of molded parts such as o-rings and gaskets for food.

Specifications/Limitations: The base fluoropolymer may be compounded with no more than 3.0 weight-percent of triallyl isocyanurate and no more than 2.5 weight-percent of 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane. Articles containing the FCS are intended to contact all food types.

A recommended description of the notification for use in FDA's public inventory is provided in **Attachment 5**.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in 21 CFR 176.170(c) Table 1, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in 21 CFR 176.170(c) Table 2, when possible.

Example: A notifier wishes to obtain approval for the use of a polymer adjuvant, Adjuvant Y, in two specific olefin polymers for use with different Food Types (see 21 CFR 176.170(c) Table 1) under different Conditions of Use (see 21 CFR 176.170(c) Table 2).

FCS/Use	Food Type	Conditions of Use
Adjuvant Y used in HDPE at levels not exceeding 0.3 wt.% of the finished polymer	Aqueous, Acidic and Low-Alcoholic (Types I, II, IVB, VIA, VIB and VIIB)	A through H
Adjuvant Y used in PP at levels not exceeding 0.2 wt.% of the finished polymer	Fatty Foods (Types III, IVA, V, VIIA, IX)	C through G

000011

Section D - INTENDED USE
2.a. - Continued

FCS/Use	Food Type	Conditions of Use

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS is intended to be used as a component of repeated use food-contact articles, primarily molded parts for food processing equipment, such as o-rings, gaskets, diaphragms, and other materials, that function primarily in sealing applications. We understand that FDA employs the assumption for such applications that 6.3×10^8 grams of food contact each square inch of o-ring, which corresponds to 4.9×10^8 g food/g o-ring.

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State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Attach data.

The FCS is a material that will be used as the basic polymer for the manufacture of molded rubber parts for food processing equipment.

Section E - STABILITY DATA
See Chemistry Recommendations Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, state none.

None.

000013

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as applicable. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

Substance Name	CAS Reg. No	Structure

000014

Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD
See Chemistry Recommendations Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any other migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5),* skip to Section II.F.2. and provide full details of all calculations.

For repeat-use articles, estimation of migrant levels in food using migration testing and/or calculations also takes into account the amount of food to contact the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4).*

1. Migration Testing Option
See Chemistry Recommendations Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). For new polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

One representative grade of the FCS was tested, (b) (4) having the following polymeric composition:

(b) (4)

The test sample was cured using triallyl isocyanurate and 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and contained 100 parts polymer, 2.5 parts triallyl isocyanurate, 2.5 parts 2,5-dimethyl-2,5-di(*tert*-butylperoxy)hexane, and 3.0 parts zinc oxide. Each sample had a thickness of 0.075 inches (75 mils) and a surface area of 43.8 in^2, and were extracted by total immersion. There are no detectable levels of any of the monomers in these polymers; detection limits for the monomers are discussed in Section II-F-2 below.

A report of the extraction study performed on ETP-600S is appended as **Attachment 6**. In this report, the Viton® ETP-600S sample is identified as Compound 1763A12-04.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food simulant volume-to-specimen surface area ratio (e.g, 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in^2). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in^2, provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

The test samples were extracted with water and hexane in a Soxhlet extractor, each solvent at its boiling point. The test samples were exposed to boiling water or boiling hexane for 7 hours, followed by a fresh aliquot of either boiling water or hexane for an additional 2 hours.

Section F - MIGRATION LEVELS IN FOOD - Continued

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components.

Example: A notifier conducted a migration study to support the use of a polymer adjuvant, Adjuvant X, intended for use at a maximum level of 0.01 wt.% in LDPE. The example table below shows how the notifier might tabulate migration data obtained from sample plaques tested in 10% ethanol under conditions of use B.

Example Table

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
LDPE containing 0.01 wt.% of Adjuvant X	Adjuvant X	10% ethanol	100°C analysis after 2 hours	0.012 mg/in² 0.011 mg/in² 0.021 mg/in²	0.015 mg/in²
			40°C analysis after 24 hours	0.015 mg/in² 0.014 mg/in² 0.022 mg/in²	0.017 mg/in²
			40°C analysis after 96 hours	0.017 mg/in² 0.017 mg/in² 0.023 mg/in²	0.019 mg/in²
			40°C analysis after 240 hours	0.020 mg/in² 0.021 mg/in² 0.023 mg/in²	0.021 mg/in²

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Part II — CHEMISTRY INFORMATION - CONTINUED

Section F - MIGRATION LEVELS IN FOOD - Continued

Summary of Migration Testing

Test Sample Formulation	Migrant	Food or Food Simulant	Temperature and time of analysis	Migration (each replicate)	Average Migration (average of replicates)
Viton® ETP-600S	Total non-volatiles	Water	Boiling/7 hours	1.35 mg/in^2	-
	Total non-volatiles	Water	Boiling/additional 2 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/7 hours	0.0 mg/in^2	-
	Total non-volatiles	Hexane	Boiling/additional 2 hours	0.0 mg/in^2	-

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Section F - MIGRATION LEVELS IN FOOD - Continued

. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of spiking procedure and calculations, must be included as an attachment.

Not applicable.

2. Migration Calculation Option

See Chemistry Recommendations Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any other migrants, such as impurities, monomers or breakdown products, in the FCS. Fully describe any assumptions made in deriving the estimates and show all calculations.

See **Attachment 7**.

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Section G- ESTIMATED DAILY INTAKE (EDI)
See Chemistry Recommendations Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any other migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult OFAS to obtain this information prior to submitting a notification.

1. Single-use Articles

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and estimated daily intake (EDI) for the FCS and any other migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Not applicable.

2. Repeat-use Articles

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any other migrants.

See **Attachment 8**.

000019

Memorandum

Date: October 14, 2005

From: Division of Food Contact Notifications
Chemistry Review Group II

Subject: FCN 000539: Keller and Heckman, LLP submission on behalf of DuPont Performance Elastomers L.L.C. Use of a copolymer of 4-bromo-3,3,4,4-tetrafluoro-1-butene, ethylene, tetrafluoroethylene and trifluoromethyl trifluorovinyl ether in the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment.

To: Division of Food Contact Notifications
Regulatory Group II
Attn: Kelly M. Randolph, D.V.M., M.P.H.

Introduction

Keller and Heckman, LLP (K&H) submitted this food contact notification (FCN 000539) on behalf of DuPont Performance Elastomers L.L.C. on July 21, 2005 (received July 25, 2005) and a subsequent update on August 28, 2005. The subject of this notification is a copolymer of 4-bromo-3,3,4,4-tetrafluoro-1-butene, ethylene, tetrafluoroethylene and trifluoromethyl trifluorovinyl ether for use in the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment, under all use conditions in contact with all types of food. The base fluoropolymer may be compounded with no more than 3.0 wt-% of triallyl isocyanurate and no more than 2.5 wt-% of 2,5-dimethyl-2,5-di(tert-butylperoxy)hexane.

The FCS is not the subject of a previous FCN. A variety of perflurocarbon cured elastomers (PCEs) have been the subject of FCNs or regulations; a summary of these compounds is provided in Attachment 1 of this memorandum. We note DuPont has submitted three previous notifications for PCEs (FCN 000101, 000510, and 000511). The notifier states that this compound is related to the PCEs notified in FCN 000510 and 000511.

The chemistry information is contained in FDA Form 3480, Attachments 1-8, and the 8-28-05 update.

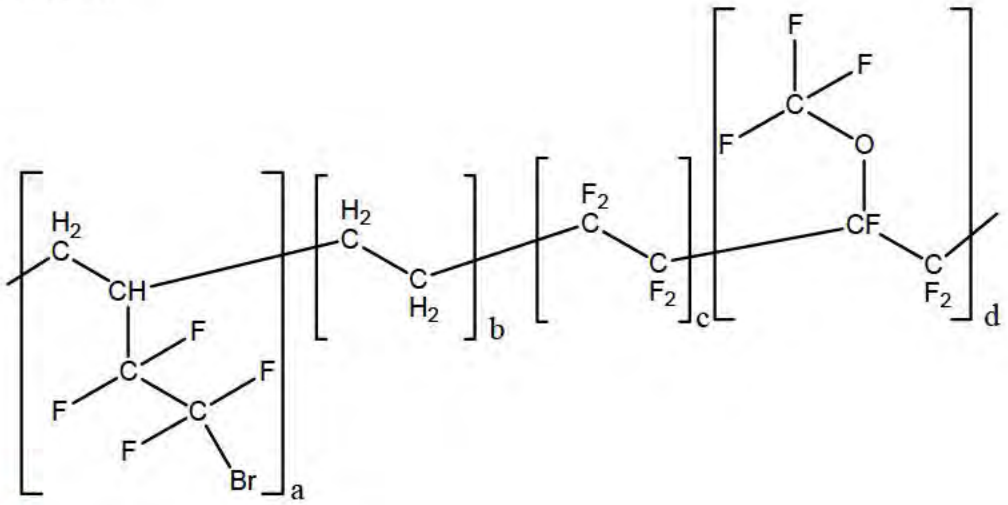
Identity of FCS

CAS name: copolymer of 4-bromo-3,3,4,4-tetrafluoro-1-butene, ethylene, tetrafluoroethylene and trifluoromethyl trifluorovinyl ether

CAS number: 105656-63-1

Other names: (b) (4)

Structure:



(b) (4)

Table 1 Physical Properties

Property	Min. Value	Max. Value
(b) (4)		

An infrared spectrum characteristic of the FCS was provided (Attachment 1).

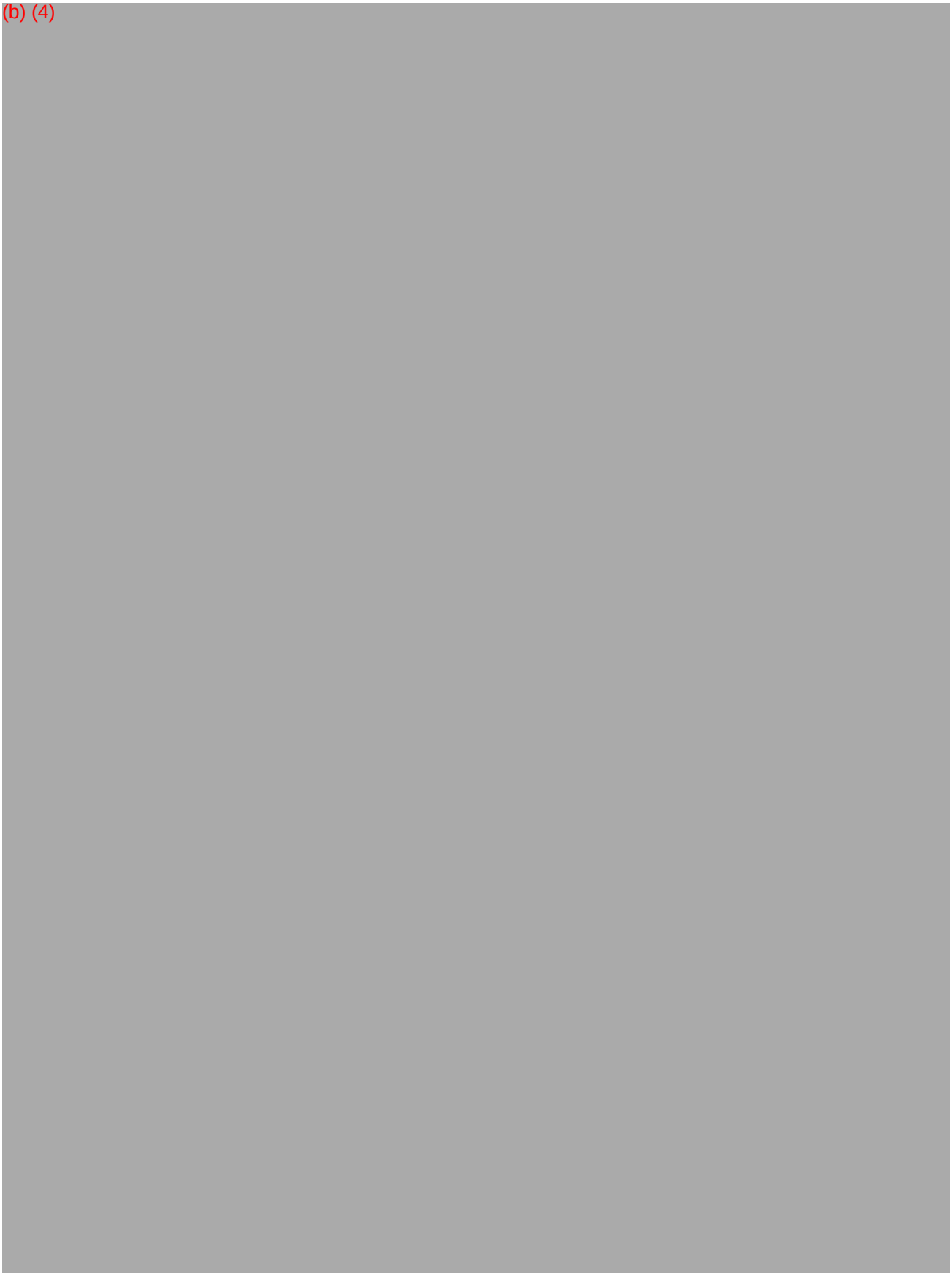
Manufacture

The manufacture is described in Form 3480 and Attachment 2. (b) (4)

(b) (4)

(b) (4)

(b) (4)



Impurities

(b) (4)

[redacted]

Table 2 Monomer Impurities

Impurity	CAS Reg. No.	Maximum Residual
(b) (4) [redacted]		

(b) (4)

[redacted]

Table 3 Manufacturing Impurities and Their Use Level

Compound	CAS Reg. No.	Use Level

(b) (4)

The notifier states that no perfluorooctane sulfonate (PFOS) is expected to be present; we concur.

The notifier analyzed a sample polymer for oligomeric material by total non-volatile extraction as described in Attachment 6. Rather than conduct migration experiments according to our "Guidance for Industry,"[1] the notifier elected to do an "exhaustive extraction" of all non-volatile materials from the polymer. The extraction study conducted by the notifier is actually the end-test extractions described in §177.2600 (Rubber articles intended for repeated use). We typically do not accept end-tests as representative of exhaustive extraction, however we have accepted these tests before for previous perfluorocarbon elastomer notifications. In this case, no detectable migrants were detected in the second extraction required by the end test. Despite performing an incorrect migration experiment, we agree that the extraction experiment does account for most of the material that would be available for migration under actual use conditions and will therefore provide a conservative estimate of exposure. Therefore, in this

[1]Guidance for Industry, Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations, Final Guidance, April 2002

case, we will accept their results. The tests and results are described below.

The notifier conducted extraction studies on (b) (4) ith a surface area of 12.56 in^2. The test samples were extracted with water and hexane in a Soxhlet extractor. The samples were refluxed for 7 hours followed by a fresh aliquot of solvent for an additional 2 hours. For each extraction, the solvent was evaporated and the resulting residue was weighed. Standard analytic techniques for exhaustive extractions include sampling at three different time periods (not two) and pooling all the samples at the end an analyzing for the total extractives. The notifier did not do this in their study. Furthermore, they report levels of 0.0 mg instead of a limit of detection (LOD). For this analysis and in lieu of requesting addition information, we will assume a limit of detection of 0.5 mg. This LOD value is a conservative estimate of the error of the balance. The results from the extraction analysis are presented below in Table 4.

Table 4 Extraction Results

Food Simulant	Time of analysis	Migration
Water	7 hours	1.35 mg/in^2
Water	Additional 2 hours	0.04 mg/$in^{2\dagger}$
Hexane	7 hours	0.04 mg/$in^{2\dagger}$
Hexane	Additional 2 hours	0.04 mg/$in^{2\dagger}$

†We assumed a limit of detection of 0.5 mg, thus the migration is 0.05 mg/12.56 in^2 = 0.04 mg/in^2.

Intended Use

The FCS is intended for use in the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment, under all use conditions in contact with all types of food. The base fluoropolymer may be compounded with no more than 3.0 wt-% of triallyl isocyanurate and no more than 2.5 wt-% of 2,5-dimethyl-2,5-di(tert-butylperoxy)hexane.

Technical Effect

This FCS will be used as the basic polymer for the manufacture of molded rubber parts for food processing equipment. The FCS exhibits high temperature and chemical resistance.

Stability

The notifier states the FCS is expected to be stable under the intended conditions of use; we concur.

Migration Studies

Migration studies were not conducted.

Exposure Estimates (tabulated below, Table 5)

Exposure to Total Non-Volatile Extractives

Exposure to the total non-volatile extractives is calculated based on the gravimetric

results from the extraction study (see Table 4, Impurities section). The water had a total of 1.39 mg/in^2 extracted (the results from the 7 hour extraction plus the 2 hour extraction, 1.35 mg/in^2 + 0.04 mg/in^2 = 1.39 mg/in^2). The exposure is calculated using a food mass-to-surface-area ratio of 6.3 x 10^8 g/in^2 as a representative of a typical o-ring application2 and assuming that 50% of all food is processed using the subject FCS. Thus the dietary concentration (DC) is calculated as follows:

$$DC = \frac{1.39\,mg\,TNE}{in^2}\ x\ \frac{1\,g}{1000\,mg}\ x\ \frac{1\,in^2}{6.3\,x10^8\ g\ food}\ x\ 0.5 = 1.1\,x10^{-12}\ g\,TNE/g\ food = 1.1\,pptr$$

The estimated daily intake (EDI) is calculated by assuming a daily diet of 3 kg food/person/day.

EDI = 3000 g food/p/d x (1.1 x 10^{-12} g TNE/g food) = 3.3 ng TNE/p/d.

Exposure to Monomers: Ethylene, TFE, and PMVE

We note that in their migration calculations for the monomers (Attachment 7, p. 85), the notifier used a value of 2.2 x 10^7 mL food/in^2 of the o-ring material. The notifier did not explain the origin of this value. Instead, we have used our standard food-mass-to-surface-area ratio. The exposure is calculated using the results from the HS-GC-MS analysis (see Table 2) and assuming the following:

1. The density of the polymer is 1.9 g/cm^3,
2. a default polymer thickness of 10 mils (0.01 in),
3. a food mass-to-surface-area ratio of 6.3 x 10^8 g/in^2,[2]
4. and that 50% of all food is processed using the subject FCS.

For example, the DC for ethylene is calculated as follows:

$$DC = \frac{26.5\,x10^{-6}\ g\ ethylene}{g\ polymer}\ x\ \frac{1.9\,g\ polymer}{1\,cm^3}\ x\ \frac{16.4\,cm^3}{1\,in^3}\ x\ 0.01\,in\ x\ \frac{1\,in^2}{6.3\,x10^8\ g\ food}\ x\ 0.5 =$$

$$6.6\,x10^{-15}\ g\ ethylene/g\ food = 6.6\ parts\ per\ quadrillion = 6.6\ ppq$$

The EDI is calculated by assuming a daily diet of 3 kg food/person/day.

EDI = 3000 g food/p/d x (6.6 x 10^{-15} g ethylene/g food) = 0.02 ng ethylene/p/d.

Exposures for TFE and PMVE are calculated as above and are tabulated in Table 5 below.

Exposures to Other Impurities

The exposures fo (b) (4) and other manufacturing impurities are based on an assumption that 100% of the impurity is present and will migrate into the food. The exposure is calculated

2Chemistry memorandum, A. Bailey to J. Smith, June 14, 1995, FAP 2B4333.

using the maximum residuals (see Table 3, note the maximum residual fo (b) (4) is 0.6%) and assuming the following:

1. The density of the polymer is 1.9 g/cm^3,
2. a default polymer thickness of 10 mils (0.01 in),
3. a food mass-to-surface-area ratio of 6.3 x 10^8 g/in^2,[2]
4. and that 50% of all food is processed using the subject FCS.

For example, the DC for (b) (4) is calculated as follows:

$$DC = \frac{0.6\,g\ \text{(b) (4)}}{100\,g\ polymer} \; x \; \frac{1.9\,g\ polymer}{1 cm^3} \; x \; \frac{16.4\,cm^3}{1 in^3} \; x \; 0.01 in \; x \; \frac{1 in^2}{6.3 x 10^8\ g\ food} \; x \; 0.5 =$$

$$1.5 x 10^{-12}\ g\ \text{(b) (4)} \,/\, g\ food = 1.5\ parts\ per\ trillion = 1.5\ pptr$$

The EDI is calculated by assuming a daily diet of 3 kg food/person/day.

EDI = 3000 g food/p/d x (1.5 x 10^{-12} g (b) (4) /g food) = 4.5 ng (b) (4) /p/d.

Exposures for other manufacturing impurities are calculated as above and presented in Table 5 below.

Exposure Summary

Exposure estimates are provided below in Table 5.

Table 5 Exposure Estimates, Dietary Concentration (DC) and Estimated Daily Intake (EDI)

Compound	CAS Reg. No.	DC	EDI
Total non-volatile extractives	n/a	1.1 pptr[▲]	3.3 ng/p/d
BTFB	18599-22-9	1.5 pptr	4.5 ng/p/d
Ethylene*	74-85-1	6.6 ppq[†]	0.02 ng/p/d
TFE*	116-14-3	0.12 ppq[†]	0.4 pg/p/d
PMVE*	1187-93-5	0.012 ppq[†]	0.04 pg/p/d
(b) (4)		2.1 pptr	6.3 ng/p/d
		0.69 pptr	2.1 ng/p/d
		2.5 pptr	7.4 ng/p/d
		1.2 pptr	3.7 ng/p/d
		0.15 pptr	0.45 ng/p/d
		2.2 ppq	6.45 pg/p/d
		0.96 ppq	2.9 pg/p/d
		0.47 ppq	1.4 pg/p/d
		0.47 ppq	1.4 pg/p/d
		0.47 ppq	1.4 pg/p/d
		0.47 ppq	1.4 pg/p/d
		0.96 ppq	2.9 pg/p/d
		7.4 pptr	22 ng/p/d
		12 pptr	37 ng/p/d

[▲]pptr = parts per trillion
[†]ppq = parts per quadrillion
*We note that in their migration calculations for the monomers (Attachment 7, p. 85), the notifier used a value of 2.2 x 10^7 mL food/in^2. We are unsure why the notifier used this value in their calculations and instead have used our standard assumption of 6.3 x 10^8 g food/in^2.

Notification Letter

The acknowledgement letter for FCN 000539, which is dated 08-04-05, is appropriate as written.

Summary

We have no questions.

Kimberly A. Smeds, Ph.D.

(b) (4)

Summary
We have no questions.

(b) (4)

Kimberly A. Smeds, Ph.D.

(b) (4)

Attachment 1- Related PCEs in regulations and notifications

§177.2400(a)

(1) … perfluorocarbon-cured elastomers are produced by terpolymerizing tetrafluoroethylene (CAS Reg. No. 116-14-3), perfluoromethyl vinyl ether (CAS Reg. No. 1187-93-5), and perfluoro-2-phenoxypropyl vinyl ether (CAS Reg. No. 24520-19-2) and subsequent curing of the terpolymer (CAS Reg. No. 26658-70-8) using the cross-linking agent, phenol, 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl) ethylidene] bis-, dipotassium salt (CAS Reg. No. 25088-69-1) and accelerator, 1,4,7,10,13,16-hexaoxacyclooctadecane (CAS Reg. No. 17455-13-9).

(2) The perfluorocarbon base polymer shall contain no less than 40 weight-percent of polymer units derived from tetrafluoroethylene, no less than 40 weight-percent of polymer units derived from perfluoromethyl vinyl ether and no more than 5 weight-percent polymer units derived from perfluoro-2-phenoxy-propyl vinyl ether.

(3) The composition limitations of the cured elastomer, calculated as parts per 100 parts of terpolymer, are as follows: Phenol, 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)-ethylidene] bis-, dipotassium salt--not to exceed 5 parts. 1,4,7,10,13,16-Hexaoxacyclo-octadecane--not to exceed 5 parts.

§177.2600(c)(4)(i)

…

Chlorotrifluoroethylene-vinylidene fluoride copolymer.

…

Vinylidene fluoride-hexafluoropropylene copolymers (minimum number average molecular weight 70,000 as determined by osmotic pressure in methyl ethyl ketone).

Vinylidene fluoride-hexafluoropropylene-tetrafluoroethylene copolymers (minimum number average molecular weight 100,000 as determined by osmotic pressure in methyl ethyl ketone).

FCN 17 (effective March 30, 2000)

A perfluorocarbon-cured elastomer (PCE) produced by terpolymerizing tetrafluoroethylene (CAS Registry No. 116-14-3), perfluoro (2,5-dimethyl-3,6-dioxanone vinyl ether) (CAS Registry No. 2599-84-0) and perfluoro (6,6-dihydro-6-iodo-3-oxa-1-hexene) (CAS Registry No. 106108-22-9) and subsequent curing of the terpolymer (CAS Registry No. 106108-23-0) by cross-linking with triallylcyanurate (CAS Registry No. 101-37-1) and vulcanizing with 2,5-dimethyl-2,5-di(t-butylperoxy)hexane (CAS Registry No. 78-63-7), as a 68% dispersion on finely divided silica.

The perfluorocarbon base polymer shall contain no less than 30 weight-percent (wt.-%) of polymer units derived from tetrafluoroethylene, no less than 60 wt.-% of polymer units derived from perfluoro(2,4-dimethyl-3,6-dioxanone vinyl ether), and no more than 4 wt.-% polymer units derived from perfluoro(6,6-dihydro-6-iodo-3-oxa-1-hexane). The uncured elastomer shall be composed of no more than 6 parts per hundred of triallylcyanurate and no more than 5 parts per hundred of 2,5-dimethyl-2,5-di(t-butylperoxy)hexane. The PCE must meet any applicable specifications prescribed in §177.2400 (Perfluorocarbon cured elastomers).

FCN 101 (effective December 19, 2000)
Perfluorocarbon cured elastomers produced by polymerizing perfluoro(methyl vinyl ether) (CAS Reg. No. 1187-93-5) with tetrafluoroethylene (CAS Reg. No. 116-14-3) and perfluoro(8-cyano-5-methyl-3,6-dioxa-1-octene) (CAS Reg. No. 69804-19-9), followed by curing with trimethylallyl isocyanurate (CAS Reg. No. 6291-95-8) and/or triallyl isocyanurate (CAS Reg. No. 1025-15-6), and with 2,5-dimethyl-2,5-di(t-butylperoxy) hexane (CAS Reg. No. 78-63-7) and as further described in this notification.

The perfluorocarbon base polymer shall contain no less than 40 weight-percent of polymer units derived from perfluoro(methyl vinyl ether), no less than 30 weight-percent of polymer units derived from tetrafluoroethylene, and no more than 5 weight-percent polymer units derived from perfluoro(8-cyano-5-methyl-3,6-dioxa-1-octene). The uncured elastomer shall be compounded with no more than 4 parts per hundred (pphr) of rubber of trimethylallyl isocyanurate and/or triallyl isocyanurate and no more than 4 pphr of 2,5-dimethyl-2,5-di(t-butylperoxy)hexane. The elastomer may also contain up to 1.0 pphr of N, N, N', N'-tetramethyl-1-8-naphthalenediamine (CAS Reg. No. 20734-58-1). The perfluorocarbon cured elastomers must meet the total extractive limitations prescribed in §177.2400(d)(1).

FCN 126 (effective July 21, 2001)
1,9-Decadiene,3,3,4,4,5,5,6,6,7,7,8,8-dodecafluoro-, polymer with tetrafluoroethene and trifluoro(trifluoromethoxy)ethene (CAS Reg. No. 190062-24-9), manufactured and characterized as further described in the notification.

The finished copolymers are intended for use as components of repeat-use, food-contact articles intended to contact food types I through VII as described in Table 1 of §176.170(c).

FCN 127 (effective July 21, 2001)
1-Propene,1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene and tetrafluoroethene (CAS Reg. No. 25190-89-0) modified with triallyl isocyanurate and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluoro-1,9-diene, manufactured and characterized as further described in the notification.

The finished copolymers are intended for use as components of gaskets or seals used in food processing equipment intended to contact food Types I through VII as described in Table 1 of §176.170(c).

FCN 128 (effective July 21, 2001)
A copolymer of tetrafluoroethylene (TFE) and perfluoromethylvinyl ether (PFMVE) (CAS Reg. No. 26425-79-6) modified with 1,3,5-triallyl isocyanurate (TAIC) and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluoro-1,9-diene, manufactured and characterized as further described in the notification.

The finished copolymers are intended for use as components of gaskets or seals used in food processing equipment intended to contact food Types I through VII as described in Table 1 of §176.170(c).

FCN 129 (effective July 21, 2001)
Ethene, tetrafluoro-, polymer with 1,1-difluoroethene and trifluoro(trifluoromethoxy)ethene (CAS Reg. No. 56357-87-0) modified with 1,3,5-triallyl isocyanurate (TAIC) and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluoro-1,9-diene, manufactured and characterized as further described in the notification.

The finished copolymers are intended for repeat use as components of gaskets or seals used in food processing equipment intended to contact food Types I through VII as described in Table 1 of §176.170(c).

FCN 245 (effective August 13, 2002)
A perfluorocarbon cured elastomer (PCE) produced by terpolymerizing tetrafluoroethylene, (CAS Reg. No. 116-14-3), perfluoromethyl vinyl ether (CAS Reg. No. 1187-93-5), and perfluoro-6,6-dihydro-6-iodo-3-oxa-1-hexane (CAS Reg. No. 106108-22-9), and subsequent curing of the terpolymer (CAS Reg. No. 193018-53-0) with triallylisocyanurate (CAS Reg. No. 1025-15-6) and 2,5-dimethyl-2,5-di(t-butylperoxy)hexane (CAS Reg. No. 78-63-7), manufactured and characterized as further described in the notification.

The FCS is intended for use in the fabrication of molded parts for food processing equipment, such as o-rings, gaskets, diaphragms and other materials that function primarily in sealing applications. he perfluorocarbon base polymer shall contain no less than 50 weight percent of polymer units derived from tetrafluoroethylene, no less than 40 weight percent of polymer units derived from perfluoromethyl vinyl ether and no more than 4 weight percent of polymer units derived from perfluoro-6,6-dihydro-6-iodo-3-oxa-1-hexene. The uncured elastomer shall be composed of no more than 6 weight percent of triallylisocyanurate, no more than 5 weight percent of 2,5-dimethyl-2,5-di(t-butylperoxy)hexane, and no more than 9 weight percent carbon black (produced by the furnace combustion process) (CAS Reg. No. 1333-86-4). The PCE must meet extractive limitations prescribed in §177.2400(d) (Perfluorocarbon cured elastomers).

FCN 246 (effective August 13, 2002)
Fluorocarbon cured elastomer produced by copolymerizing tetrafluoroethylene (CAS Reg. No. 116-14-3) and propylene (CAS Reg. No. 115-07-01) and subsequent curing of the copolymer (CAS Reg. No. 27029-05-6) with triallylisocyanurate (CAS Reg. No. 1025-15-6) and 2,2' bis-(t-butylperoxy)diisopropylbenzene (CAS Reg. No. 25155-25-3), manufactured and characterized as further described in the notification.

The FCS is intended for use in the fabrication of molded parts for food processing equipment, such as o-rings, gaskets, diaphragms and other materials that function primarily in sealing applications. The fluorocarbon base polymer shall contain no less than 65 weight percent of polymer units derived from tetrafluoroethylene and no less than 25 weight percent of polymer units derived from propylene. The uncured elastomer shall be composed of no more than 6 weight percent of triallylisocyanurate and no more than 5 weight percent of 2,2'-bis(t-butylperoxy)diisopropylbenzene, and no more than 15 weight percent carbon black (produced by the furnace combustion process) (CAS Reg. No. 1333-86-4). The PCE must comply with the provisions of §177.2600 (Rubber articles intended for repeated use)(d) and (g) and the extractive limitations prescribed in §177.2600(e) and (f), and §177.2400(d)(2)(Perfluorocarbon cured

elastomers).

FCN 247 (effective August 13, 2002)
A perfluorocarbon cured elastomer (PCE) produced by terpolymerizing tetrafluoroethylene, (CAS Reg. No. 116-14-3), perfluoro-2,5-dimethyl-3,6-dioxanonane vinyl ether (CAS Reg. No. 2599-84-0), and perfluoro-6,6-dihydro-6-iodo-3-oxa-1-hexene (CAS Reg. No. 106108-22-9), and subsequent curing of the terpolymer (CAS Reg. No. 106108-23-0) with triallylisocyanurate (CAS Reg. No. 1025-15-6) and 2,5-dimethyl-2,5-di(t-butylperoxy)hexane (CAS Reg. No. 78-63-7), manufactured and characterized as further described in the notification.

The FCS is intended for use in the fabrication of molded parts for food processing equipment, such as o-rings, gaskets, diaphragms and other materials that function primarily in sealing applications. The perfluorocarbon base polymer shall contain no less than 30 weight percent of polymer units derived from tetrafluoroethylene, no less than 60 weight percent of polymer units derived from perfluoro-2,5-dimethyl-3,6-dioxanonane vinyl ether and no more than 4 weight percent of polymer units derived from perfluoro-6,6-dihydro-6-iodo-3-oxa-1-hexene. The uncured elastomer shall be composed of no more than 6 weight percent of triallylisocyanurate, no more than 5 weight percent of 2,5-dimethyl-2,5-di(t-butylperoxy)hexane, and no more than 12 weight percent carbon black (produced by the furnace combustion process) (CAS Reg. No. 1333-86-4). The PCE must meet extractive limitations prescribed in §177.2400(d) (Perfluorocarbon cured elastomers).

FCN 278 (effective November 27, 2002)
Copolymer of tetrafluoroethylene, perfluoromethylvinylether and 1-iodo-2- bromo-tetrafluoroethane intended to be cross-linked with triallylisocyanurate, manufactured and characterized as further described in the notification.

The FCS is intended for use as an o-ring or gasket in food-processing machinery for use in all food types up to 120 ºC.

FCN 481 (effective May 10, 2005)
1-Hexene, 3,3,4,4,5,5,6,6,6-nonafluoro-, polymer with ethane and tetrafluoroethene (CAS Reg. No. 68258-85-5), manufactured and characterized as further described in the notification.

The FCS is intended for use as a base polymer or coating in repeat-use applications at temperatures up to 302 ºF (150 ºC). Specific applications include use in storage tanks and mobile road tankers, food transport pipes and delivery tubes, butterfly valves, lined housing, feeding hoppers, sieves, o-rings and seals.

FCN 510 (b) (4)
Copolymer of 1,1-difluoroethylene, hexafluoropropene, tetrafluoroethylene, and a halogenated alkene, optionally cured with triallyl isocyanurate, 2,5-dimethyl-2,5-di(tertbutylperoxy)hexane, and/or zinc oxide, manufactured and characterized as further described in the notification.

The FCS is intended for repeat-use in the fabrication of molded parts such as o-rings and gaskets for food processing equipment. The base fluoropolymers may be compounded with no more

than 3.0 wt-% of triallyl isocyanurate and no more than 2.5 wt-% zinc oxide. Articles containing the FCS are intended to contact all food types.

FCN 511 (b) (4)

Copolymer of 1,1-difluoroethylene, tetrafluoroethylene, trifluoromethyl trifluorovinyl ether and a halogenated alkene, optionally cured with triallyl isocyanurate, 2,5-dimethyl-2,5-di(tertbutylperoxy)hexane, and/or zinc oxide, manufactured and characterized as further described in the notification.

The FCS is intended for repeat-use in the fabrication of molded parts such as o-rings and gaskets for food processing equipment. The base fluoropolymers may be compounded with no more than 3.0 wt-% of triallyl isocyanurate and no more than 2.5 wt-% zinc oxide. Articles containing the FCS are intended to contact all food types.

CHEMOURS FCN 598

FORM 3480 WAS MISSING
FROM THE FOIA RESPONSE

FOR USE IN REPEATE-USE
FOOD CONTACT ARTICLES

Memorandum

Date: March 6, 2006

From: Division of Food Contact Notifications
Chemistry Review Group II

Subject: FCN 000598: Keller and Heckman, LLP submission on behalf of DuPont Performance Elastomers, LLC dated December 28, 2005. Use of a copolymer of propylene, tetrafluoroethylene and 3,3,3-trifluoropropene compound with no more than 3.0 wt-% of a curing agent for use in the fabrication of molded parts of food processing machinery for repeated use in contact with all food types.

To: Division of Food Contact Notifications
Regulatory Group II
Attn: Vivian Gilliam

Introduction

Keller and Heckman, LLP (K&H) submitted this food-contact substance notification (FCN 000598) on behalf of DuPont Performance Elastomers, LLC on December 28, 2005 (received December 30, 2005) and a subsequent update on February 14, 2006.[1] This notification is for the use of a copolymer of propylene, tetrafluoroethylene and 3,3,3-trifluoropropene compound with no more than (b)(4) and/or (b)(6) curing agent in the fabrication of molded parts of food processing machinery for repeated use in contact with all food types.

The FCS is not the subject of a previous FCN. A variety of perfluorocarbon-cured elastomers (PCEs) have been the subject of FCNs or regulations; a summary of these compounds is provided in Attachment 1 of this memorandum. We note that DuPont has submitted four previous FCNs for PCEs (FCN 000101, 000510, 000511, and 000539).

The chemistry information is contained in FDA Form 3480, Attachments 1-8, and the 2-14-06 update.

Identity of FCS

CAS name: a copolymer of propylene (CAS Reg. No. 115-07-1), tetrafluoroethylene (TFE, CAS Reg. No. 116-14-3), and 3,3,3-trifluoropropene (TFP, CAS Reg. No. 677-21-4) cured with (b)(4) and/or (b)(6)

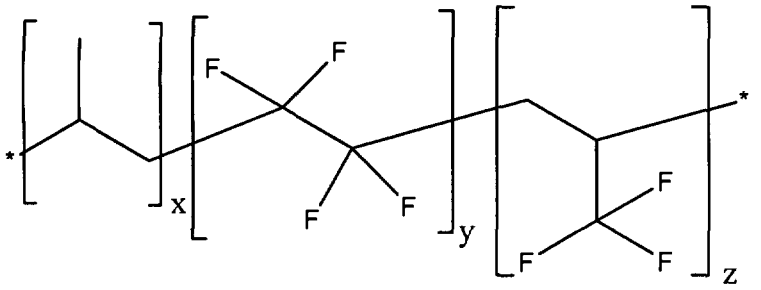
CAS number: 475654-94-5

[1]Correspondence letter, Jerome H. Heckman (K&H) to Vivian Gilliam (FDA), February 14, 2006, Response to FDA's Questions on Food Contact Notifications No. 598.

000580

Other names: (b)(4) and/or (b)(6)

Structure:



where x = 16 – 20 wt-%, y = 76 – 80 wt-%; and z = 4 – 5 wt-%.

We note the notifier provided the composition of a "representative" polymer product. (b)(4) and/or (b)(6) This polymer, cured with 3.0 wt-% tributylmethylammonium 4,4-[trifluoromethyl]ethylidene]diphenol salt comprises the test samples for the extraction studies.

Molecular weight: The notifier states that the FCS is insoluble and, therefore it is not possible to perform GPC analyses for molecular weight information.

Physical properties: Physical property data is provided in Attachment 4. For the polymer only the volatile loss at 130 °C is a maximum of 0.5 wt-% and the Mooney viscosity at 121 °C is 46.0 – 64.0. For the polymer plus curatives the volatile loss at 130 °C is a maximum of 1.0 wt-% and the Mooney viscosity at 121 °C is 45.0 – 65.0.

An infrared spectrum characteristic of the FCS was provided (Attachment 1).

Manufacture

(b)(4) and/or (b)(6)

(b)(4) and/or (b)(6)

Impurities

(b)(4) and/or (b)(6)

The notifier did not analyze the sample for residual non-monomer components that are used in the manufacture. The notifier states that these substances will be, to a large extent, removed during the manufacturing process when the polymer crumb is washed, filtered, and dried. However, since the polymer was not analyzed for these compounds, the notifier bases their exposure on a 100% migration assumption. We agree with this conservative assumption. The identity of these substances and their use levels are provided below in Table 1.

Table 1 Manufacturing Impurities

Substance	CAS Reg. No.	Use Level
(b)(4) and/or (b)(6)		4.15 %
		5.5 %
		3.0 %
		0.79%
		3.0 %

(b)(4) and/or (b)(6)

The notifier analyzed a sample polymer for oligomeric material by total non-volatile extraction as described in Attachment 6. Rather than conduct migration experiments according to our "Guidance for Industry,"[2] the notifier elected to do an "exhaustive extraction" of all non-volatile materials from the polymer. The extraction study conducted by the notifier is actually the end-test extractions described in §177.2600 (Rubber articles intended for repeated use). We typically do not accept end-tests as representative of exhaustive extraction; however we have accepted these tests before for previous perfluorocarbon elastomer notifications. In this case, no detectable migrants were detected in the second extraction required by the end test. Despite performing an incorrect migration experiment, we agree that the extraction experiment does, in this specific case, account for most of the material that would be available for migration under actual use conditions and will therefore provide an adequate estimate of exposure. The tests and results are described below. One question on the extraction study arose during the preliminary review of this FCN. From experience in our laboratories, we knew that depending on their structure, fluorinated low molecular weight oligomers may be very difficult to analyze. To determine whether the analytical procedure was correctly conducted, we asked whether the extraction solvent was removed from the test vial, evaporated and then weighed, or whether the solvent was evaporated in the original test vial and then weighed. If the solvent had been transferred from one vessel to another, the notifier would have had to perform spike and recovery validation of their procedure to determine transfer loss of fluorooligomers. In their 2-14-06 update the notifier did not address this question. Instead, for exposure estimates, they chose to rely on an assumption that 10% of the FCS consists of oligomers and that 100% of this fraction actually migrates to the contacted food. We agree that this assumption will provide a conservative exposure estimate, and we will use the 10% oligomer assumption in our exposure estimate.

[2]Guidance for Industry, Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations, Final Guidance, April 2002

The notifier conducted extraction studies on (b)(4) and/or (b)(6) with a surface area of 43.8 in^2. The test samples were extracted with water and hexane in a Soxhlet extractor. The samples were extracted for 7 hours after which a fresh aliquot of solvent was added and refluxed for an additional 2 hours. For each extraction, the solvent was evaporated and the resulting residue was weighed. Standard analytical techniques for exhaustive extractions include sampling at three different time periods (not two) and pooling all the samples at the end an analyzing for the total extractives. The notifier did not do this in their study. Furthermore, they report levels of 0.0 mg instead of a limit of detection (LOD). In their 2-14-06 update, the notifier provided a limit of detection of 0.01 mg which we will use in estimating migration for those substances not detected. The results from the extraction analysis are presented below in Table 2.

Table 2 Extraction Results

Test Sample	Food Simulant	Time of analysis	Migration
(b)(4) and/or (b)(6) processed with 8 parts MgO	Water	7 hours	1.62 mg/in^2
	Water	Additional 2 hours	0.0008 $mg/in^{2\dagger}$
	Hexane	7 hours	1.74 mg/in^2
	Hexane	Additional 2 hours	0.0008 $mg/in^{2\dagger}$
(b)(4) and/or (b)(6) processed with 6 parts MgO	Water	7 hours	0.0008 $mg/in^{2\dagger}$
	Water	Additional 2 hours	0.0008 $mg/in^{2\dagger}$
	Hexane	7 hours	0.47 mg/in^2
	Hexane	Additional 2 hours	0.0008 $mg/in^{2\dagger}$

†Limit of detection = 0.01 mg, thus the migration is 0.01 mg/12.56 in^2 = 0.0008 mg/in^2.

Intended Use

The FCS is intended for use in the fabrication of molded parts intended for repeated use, such as o-rings and gaskets for food processing equipment, under all use conditions in contact with all types of food.

Technical Effect

This FCS will be used as the basic polymer for the manufacture of molded rubber parts for food processing equipment. The FCS exhibits high temperature and chemical resistance.

Stability

The notifier states the FCS is expected to be stable under the intended conditions of use; we concur.

Migration Studies

Migration studies were not conducted.

Exposure Estimates (tabulated below, Table 3)

Exposure to the FCS

We typically assume that 6.3 x 10^8 g of food contact each square inch of o-ring.[3] On p. 8 of Form 3480, the notifier states that 6.3 x 10^8 g of food/in^2 of o-ring corresponds to 4.9 x 10^8 g food/g o-ring. Thus the maximum level of potential migration of oligomers is (0.1 g oligomers/g polymer)/(4.9 x 10^8 g food/g polymer) = 0.2 ppb. The dietary concentration may be calculated by assuming that 50% of all food is processed using the subject FCS. Thus the dietary concentration (DC) is calculated as follows:

DC = 0.5 x 0.2 ppb = 0.1 ppb

The estimated daily intake (EDI) is calculated by assuming a daily diet of 3 kg food/person/day.

EDI = 3000 g food/p/d x (0.1 x 10^{-9} g oligomers/g food) = 0.3 µg TNE/p/d.

Exposure to Monomers: Propylene, TFE, and TFP

The exposure is calculated using the results from the HS-GC-MS analysis (see Impurities Section) and assuming the following:

1. The density of the polymer is 1.9 g/cm^3,
2. a default polymer thickness of 10 mils (0.01 in),
3. a food mass-to-surface-area ratio of 6.3 x 10^8 g/in^2,[3]
4. and that 50% of all food is processed using the subject FCS.

For example, the DC for propylene is calculated as follows:

$$DC = \frac{16.9 x 10^{-9}\ g\ propylene}{g\ polymer} x \frac{1.9\ g\ polymer}{1 cm^3} x \frac{16.4 cm^3}{1 in^3} x\ 0.01 in\ x \frac{1 in^2}{6.3 x 10^8\ g\ food} x\ 0.5 =$$

$$4.2 x 10^{-18}\ g\ ethylene / g\ food = 4.2\ parts\ per\ quintillion = 6.6\ ppqt$$

The EDI is calculated by assuming a daily diet of 3 kg food/person/day.

EDI = 3000 g food/p/d x (4.2 x 10^{-18} g propylene/g food) = 0.12 fg propylene/p/d.

Exposures for TFE and TFP are calculated as above and are tabulated in Table 3 below.

Exposures to Other Impurities

The exposures for other manufacturing impurities (see Table 1) are based on an assumption that 100% of the impurity is present and will migrate into the food. The exposure is calculated using the maximum residuals (Table 1) and assuming the following:

---

[3]Chemistry memorandum, A. Bailey to J. Smith, June 14, 1995, FAP 2B4333.

1. The density of the polymer is 1.9 g/cm^3,
2. a default polymer thickness of 10 mils (0.01 in),
3. a food mass-to-surface-area ratio of 6.3 x 10^8 g/in^2,[3]
4. and that 50% of all food is processed using the subject FCS.

(b)(4) and/or (b)(6)

Exposures for other manufacturing impurities are calculated as above and presented in Table 3 below.

Exposure Summary

Exposure estimates are provided below in Table 3.

Table 3 Exposure Estimates: Dietary Concentration (DC) and Estimated Daily Intake (EDI)

Substance	CAS Reg. No.	DC	EDI
FCS	n/a	0.1 ppb	0.3 µg/p/d
Propylene	115-07-1	4.1 ppqt	0.12 fg/p/d
TFE	116-14-3	0.47 ppq	1.4 pg/p/d
TFP	677-21-4	8.2 ppqt	0.27 fg/p/d
(b)(4) and/or (b)(6)			31 ng/p/d
			41 ng/p/d
			22 ng/p/d
			5.9 ng/p/d
			22 ng/p/d

pptr = parts per trillion (10^{-12}); ppq = parts per quadrillion (10^{-15}); ppqt = parts per quintillion (10^{-18}); ng = nanogram (10^{-9}); pg = pictogram (10^{-12}); fg = femtogram (10^{-15})

Notification Letter

The acknowledgement letter for FCN 000598, which chemistry signed on 02-23-06, is appropriate as written.

Summary

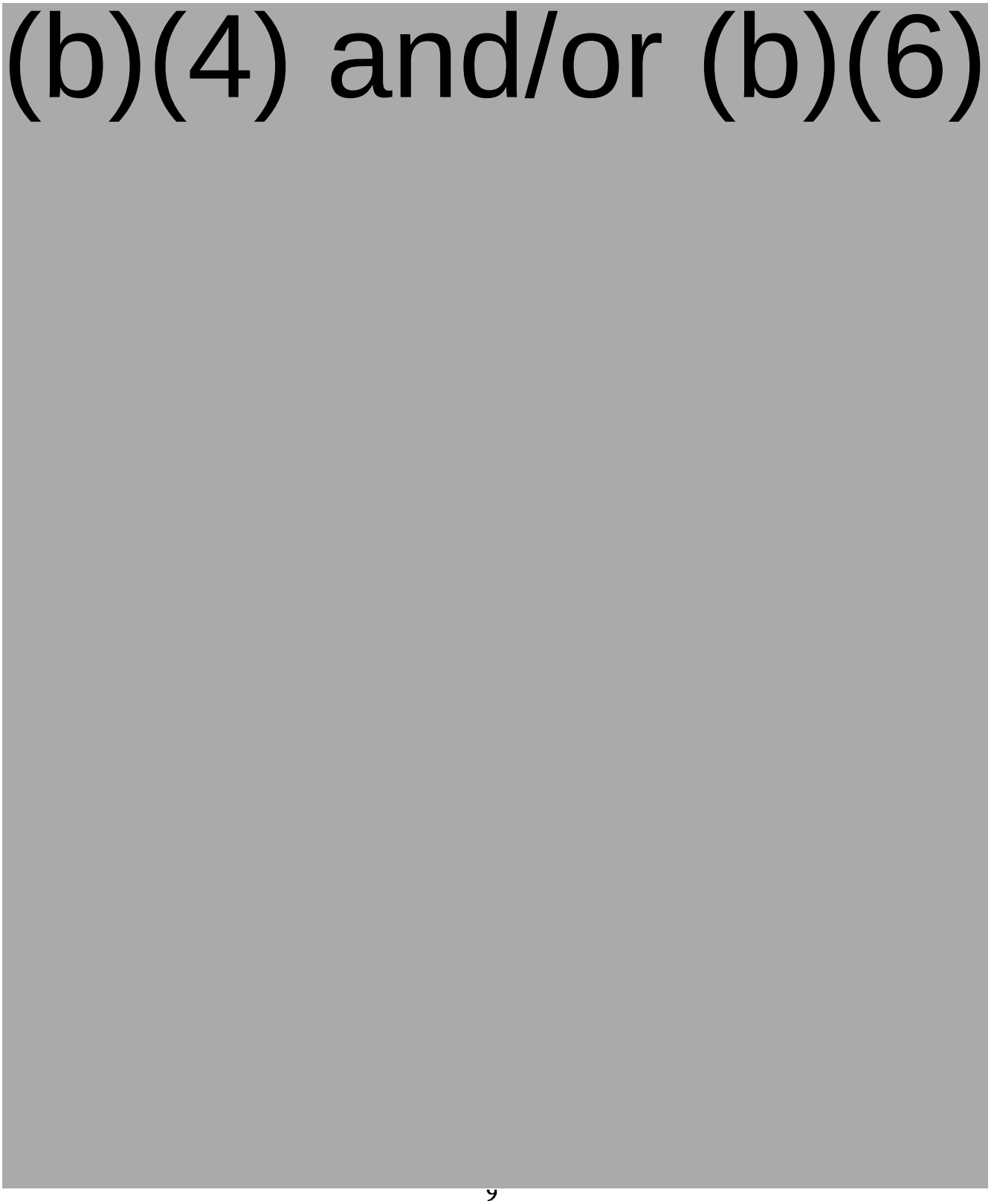
We have no questions.

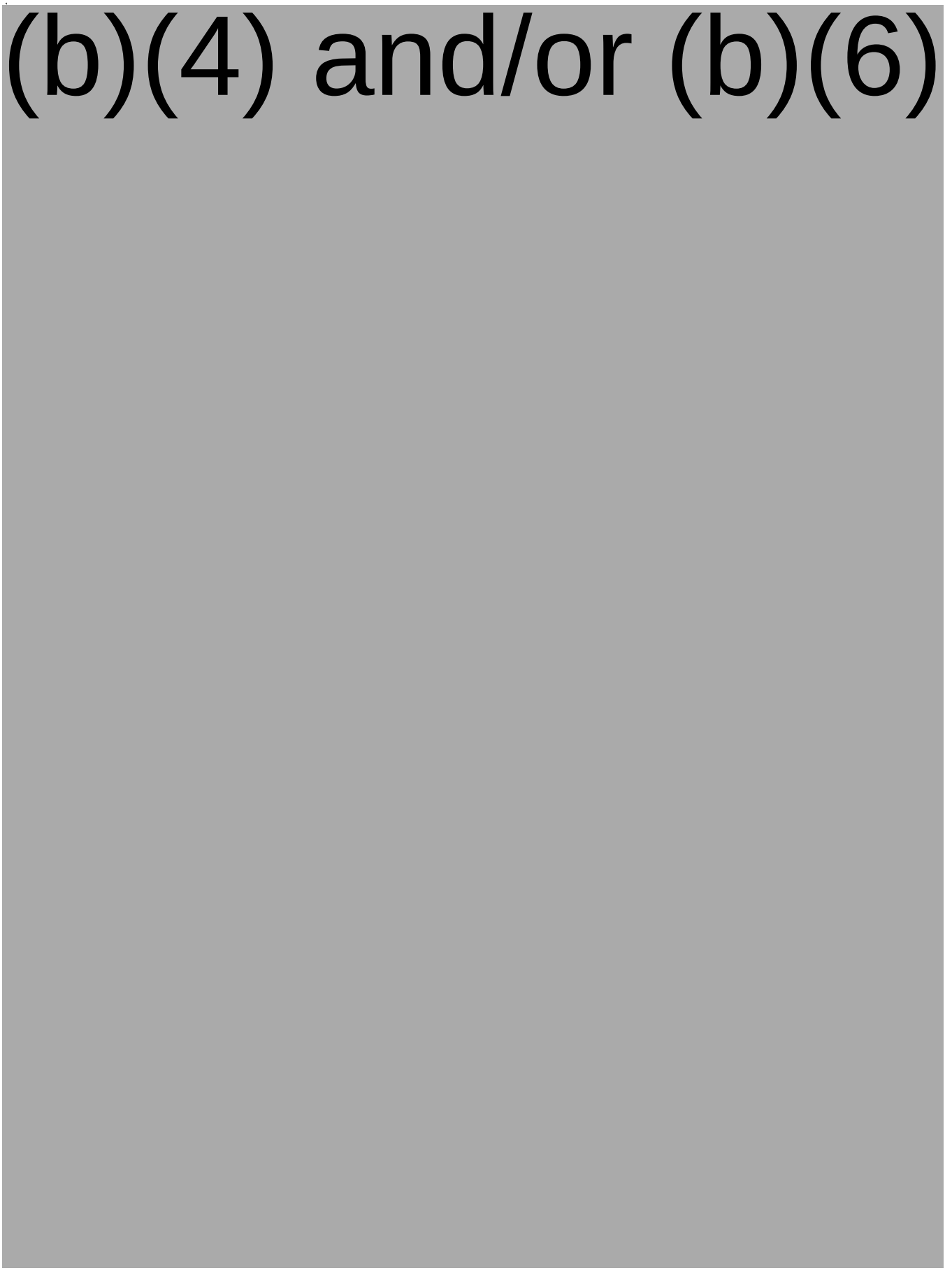
(b)(4) and/or (b)(6)

Kimberly A. Smeds, Ph.D.

(b)(4) and/or (b)(6)

Attachment 1- Related PCEs in regulations and notifications

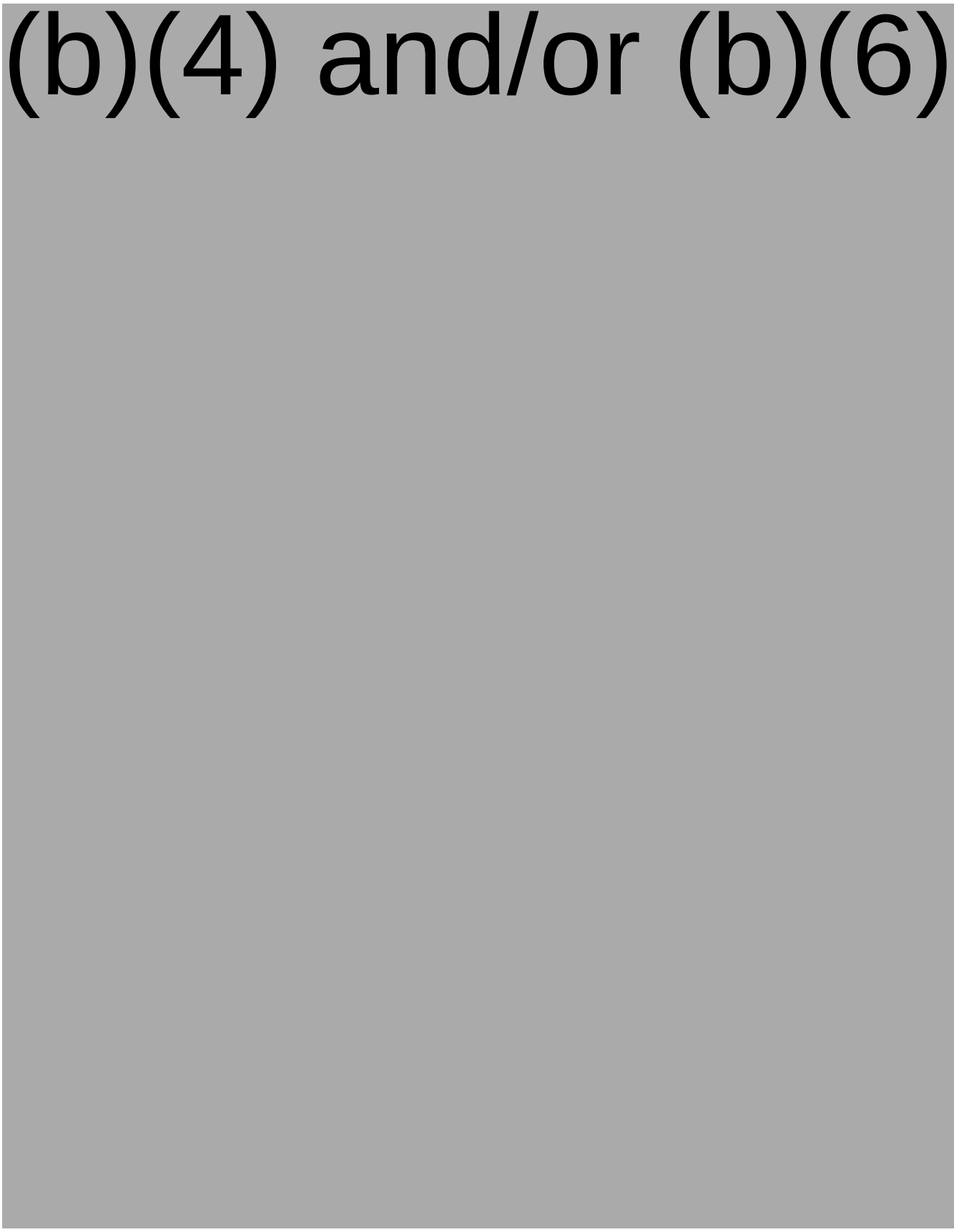



(b)(4) and/or (b)(6)

(b)(4) and/or (b)(6)

(b)(4) and/or (b)(6)

(b)(4) and/or (b)(6)


(b)(4) and/or (b)(6)

(b)(4) and/or (b)(6)

CHEMOURS FCN 947

FOR USE IN REPEATE-USE
FOOD CONTACT ARTICLES

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with tetrafluoroethene

2. CAS Registry Number

25067-11-2

3. Trade or Common Name

FEP polymer; Fluorinated Ethylene Propylene copolymer

4. Other Chemical Names *(IUPAC, etc.)*

copolymer of hexafluoropropylene, tetrafluoroethene, and perfluoroethyl vinyl ether;
hexafluoropropene polymer with tetrafluoroethylene

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The different polymer "grades" have different specifications, and A, B, C, and D represent different manufacturing processes. The following are representative grades:

Polymer "Grades"	Perfluoroethyl vinyl ether (PEVE) (%)	Hexafluoropropylene (HFP) (%)	Tetrafluoroethylene (TFE)
	(b) (4)		
(b) (4)			Balance
			Balance
			Balance
			Balance
			Balance
			Balance
			Balance
			Balance

☐ you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See FTIR spectra in **Attachment 1**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
See Attachment 2			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See manufacturing process descriptions and lists of process ingredients in **Attachment 3**.

Also included with this attachment is a description of processing steps which may occur when the materials of interest are used in a particular application – in this case, a coatings application. This level of detail is included to help more fully describe the complete process sequence the materials may experience in this type of unique application.

☐

Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
Tetrafluoroethylene (TFE)	116-14-3	<0.001 ppm	-	☒ Yes ☐ No
Hexafluoropropylene (HFP)	116-15-4	0.002-0.018 ppm	-	☒ Yes ☐ No
Perfluoroethylvinyl ether (PEVE)	10493-43-3	0.001 ppm	-	☒ Yes ☐ No
(b) (4) [redacted]		0.02-0.42 ppm	-	☒ Yes ☐ No
		7.2-15 ppm	-	☒ Yes ☐ No
		0.0351	-	☒ Yes ☐ No
			-	☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

See **Attachment 4** for residual monomer report.

See **Attachment 5** for residual (b) (4) [redacted]

See **Attachment 6** for (b) (4) [redacted] analysis report.

See **Attachment 7** for kinetics of decomposition and recombination of initiator report.

See **Attachment 14** for discussion regarding the expected absence of (b) (4) [redacted] in the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS

See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
See Attachment 8	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distribution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS. **See Attachment 9 for specification test methods.**

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
See Attachment 8			

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

The molecular weight distribution of the FCS cannot be determined, as the polymer is not soluble in any solvents in which molecular weight determination can be performed. Thus, the molecular weight distribution is not known.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☐ Single Use ☒ Repeat Use

The food-contact substance (FCS) will be used in repeated-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings. The coatings will have a maximum thickness of 15 mils.

Proposed language for listing on FDA's "Inventory of Effective Food Contact Substance Notifications" website is provided in **Attachment 11**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS will be used in repeated-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings. The FCS will contact all food types under Conditions of Use A through H, and J.

As an example of articles, tubing may have a diameter of 0.25 – 10 inches, and is expected to have a useful life of 5 – 10 years. With regard to coatings, they will have a maximum thickness of 15 mils and may be comprised entirely of the FCS. The coatings may be used on metal bakeware/cookware for cooking applications, and for coatings on metal pipe linings. We have developed representative use scenarios for bakeware/cookware and pipes.

A representative size bakeware/cookware container is one that has dimensions of 3 inches in height, 8 inches wide, and 10 inches long. When filled within 0.25 inch of the top, the volume is calculated to be 2.75 in x 8 in x 10 in = 220 in^3 = 3608 cm^3 = 3608 g food (assuming a density of 1 g/cm^3); the internal food-contact surface area is calculated to be approximately 179 in^2. Thus, the food mass-to-surface area ratio for each use would be (3608 g) ÷ (179 in^2) = 20 g/in^2. Therefore, a typical amount of food contacted over the service life of the article is expected to be approximately 1000 x 20 g/in^2 = 2.0 x 10^4 g food/in^2.

The pipes will have approximate diameters of 2 – 4 inches with a length of 20 – 40 feet; some pipes may have diameters of up to 8 inches with lengths of up to 100 feet. The flow rate in a 6-inch diameter pipe will be approximately 150 million pounds per year. The coatings are expected to have a useful life of 5 – 10 years. The 6 inch pipe is employed as a useful representative to calculate the food-to-surface area ratio. The circumference of a 6 inch circle is 18.9 in, and the surface area of a 100 foot length is (18.9 in) x (100 ft) x (12 in/ft) = 22,680 in^2. Over the minimum expected lifetime, the total amount of food would be (150 x 10^6 lb/year) x (454 g/lb) x (5 years) = 3.41 x 10^{11} g. Therefore, the food mass-to-surface area ratio over the lifetime is (3.41 x 10^{11} g) ÷ (22,680 in^2) = 1.5 x 10^7 g/in^2.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

See **Attachment 12** for representative product information sheets.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

   No degradation is expected. See Thermogravimetric Analysis (TgA) data in **Attachment 13**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
STRUCTURE		**STRUCTURE**	

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.

STRUCTURE	STRUCTURE

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Not applicable.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of sp king procedure and calculations, must be included as an attachment.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully descr be assumptions made in deriving the estimates and show all calculations.

See migration calculations in **Attachment 14**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly describe the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information described in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

See dietary exposure calculations in **Attachment 15**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
FCS (Oligomers)	25067-11-2	3.2	0.16	0.00048	0.16
Tetrafluoroethylene (TFE)	116-14-3	0.000018	0.0000009	2.7×10^{-9}	-
Hexafluoropropylene (HFP)	116-15-4	0.00032	0.000016	4.8×10^{-8}	-
Perfluoroethylvinyl ether (PEVE)	10493-43-3	0.000018	0.0000009	2.7×10^{-9}	-
(b) (4) [redacted]		0.0074	0.00037	1.1×10^{-6}	-
		0.26	0.013	3.9×10^{-5}	-

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: March 22, 2010

From: Division of Food Contact Notifications
Chemistry Team II

Subject: FCN 947: Use of 1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1,2,2-tetrafluoroethene and 1,1,2-trifluoro-2-(1,1,2,2-pentafluoroethoxy)ethene in repeated use food contact articles. The food-contact substance (FCS) is intended to contact all food types under Conditions of Use A-H, and J.

To: Division of Food Contact Notifications
Regulatory Team II
Attn: M. Hepp, Ph.D.

DuPont Chemical Solutions Enterprise, through Keller and Heckman, L.L.C., submitted this food contact notification (FCN) dated 10/26/2009 and updated on 12/11/2009 and 12/31/2009 for the use of 1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1,2,2-tetrafluoroethene and 1,1,2-trifluoro-2-(1,1,2,2-pentafluoroethoxy)ethene in repeated use food contact articles. The food-contact substance (FCS) is intended to contact all food types under Conditions of Use A-H, and J.

Background and Regulatory Status of the FCS

The FCS is not currently regulated for use in contact with food; however, similar materials are regulated under 177.1550 (Perfluorocarbon resins). There are currently no authorized uses for the FCS in contact with food. There are four perfluoropolymer containing 1-propene, 1,1,2,3,3,3-hexafluoropropene listed on the web page of effective notifications.

FCN 127: 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene and tetrafluoroethene (CAS Reg. No. 25190-89-0) modified with triallyl isocyanurate and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodeca-1,9-diene for use as a gasket or seal for food processing equipment.

FCN 260: Tetrafluoroethylene-hexafluoropropylene-vinylidene fluoride copolymers (CAS Reg. No. 25190-89-0) for use as a processing additive for polyolefins in contact with food.

FCN 510: Copolymer of 1,1-difluoroethylene, hexafluoropropene, tetrafluoroethylene, and iodotetrafluorobutene, optionally cured with triallyl isocyanurate and 2,5-dimethyl-2,5-di(tert-butylperoxy)hexane. For use in the fabrication of repeat-use molded parts such as o-rings and gaskets for food processing equipment.

FCN 736: 1-Propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1-difluoroethene (CAS Reg. No. 9011-17-0) modified with a 2-bromo-1,1-difluoroethylene (CAS Reg. No. 33831-83-3) for use as a processing additive for all polymers in contact with all food types.

Identity

We do not agree with the name or CAS registry number (CAS RN) supplied by the notifier for the FCS. This name does not take into account the presence of the third monomer (1,1,2-trifluoro-2-(1,1,2,2-pentafluoroethoxy)ethane) in the FCS. We searched CAS and found the correct name and CAS number for this FCS. The notifier provided comments on this requested change in identity in their 12/11/2009 update to the notification. The notifier states that 1,1,2-trifluoro-2-(1,1,2,2-pentafluoroethoxy)ethane is used at a level below 2 weight-percent and is not subject to identification under the Toxic Substance Control Act, therefore, the notifier wishes to use CAS number 25067-11-2 to identify this material. We do not agree with the notifier that the CAS RN 25067-11-2 adequately describes the FCS in that this CAS RN is clearly assigned to the copolymer of hexafluoropropylene (HFP) and tetrafluoroethene (TFE). In addition, the TSCA rules do not apply to the identification of food-contact materials for regulatory purposes of the FDA; therefore, all monomers must be accounted for in the identifying name. As such, FDA will refer to and index this material:

CAS Name: 1-propene, 1,1,2,3,3,3-hexafluoro-, polymer with 1,1,2,2-tetrafluoroethene and 1,1,2-trifluoro-2-(1,1,2,2-pentafluoroethoxy)ethene

CAS Reg. No.: 63654-40-0
Trade Names: FEP polymer; fluorinated ethylene propylene copolymer

Other Names: Copolymer of hexafluoropropylene, tetrafluoroethene, and perfluoroethyl vinyl ether

For purposes of listing the FCS on the web page of effective notifications, the notifier's suggested language (copolymer of hexafluoropropylene (CAS RN 116-15-4),tetrafluoroethene (CAS RN 116-14-3), and perfluoroethyl vinyl ether (CAS RN 10493-43-3)) is acceptable.

The notifier states that the FCS is not soluble in any solvents in which molecular weight determinations can be performed. However, the notifier provided other specifications (melt flow index values) in Attachment 8 of the FCN that can be used to distinguish the different grades of the FCS. The notifier did not provide the volatiles index values for resins (b) (4) [redacted] In the notifier's 12/11/2009 update to the notification, they state the resins (b) (4) [redacted] do not have volatiles index values as part of their specifications.

The following table identifies representative grades of the FCS. The A, B, C, and D designations represent different manufacturing processes.

Polymer "Grades"	Perfluoroethyl vinyl ether (PEVE) (%)	Hexafluoropropylene (HFP) (%)	Tetrafluoroethylene (TFE)
polymer (b) (4)	(b) (4)		
polymer			
polymer			
polymer			
polymer			
polymer			
polymer			

The notifier provided an IR spectrum of the FCS in Attachment 1 of the notification. The spectrum is consistent with that of a perfluorinated polymer.

Stability

DuPont included a thermogravimetric analysis (TGA) of the FCS (Attachment 13). Samples were heated to 177°C (350 °F) in air and held for 120 minutes. In our 11/27/2009 deficiency letter, we requested thermogravimetric data (TGA) demonstrating the stability of the polymer at temperatures of up to 230°C (typical frying temperature). DuPont provided the requested TGA data in their 12/11/2009 update to the notification (Attachment 1). While it is not the type of scan we had anticipated (polymer weight as a function of temperature), it does show stability and, given the low exposures expected from these repeat uses, it is acceptable.

Manufacture

Polymerization

The notifier provided detailed data on the manufacture of the FCS in Attachment 3 of the FCN. (b) (4)

(b) (4)

(b) (4)


(b) (4)


(b) (4)


(b) (4)


(b) (4)


(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Intended Use/Use Level and Intended Technical Effect

The FCS will be used in repeated-use food-contact applications, such as articles (tubing, tanks, for food equipment), coatings on metal bake ware and cookware, and metal pipe linings (maximum thickness of coating to be 15 mils). The FCS will contact all food types under Conditions of Use A-H and J. From the information provided in the notification, the intended use of this material will be substitutional for those regulated under 177.1550.

Migration Studies

The notifier did not conduct migration studies in support of this notification. Instead, they analyzed the finished food contact substance for oligomers and impurities and used these values and 100% migration calculations to estimate exposure to the FCS and its impurities.

Low-molecular weight oligomers

The notifier states that they conducted exhaustive extractions of resin (b) (4) (a resin covered by FCN 948) and [redacted] a resin covered by this FCN) using 95% ethanol. A review of these data demonstrates that there was still material being extracted from the resin during the second extraction of the FCS using fresh 95% ethanol. Using appropriate analytical technique, the notifier should have continued with the extractions until no additional material was recovered

from the resin. In addition, it appears that the notifier only extracted one of the 4 types of the FCS requested under this FCN, resin (b) (4). In our 11/27/2009 deficiency letter, we requested that the notifier comment on the design of the extraction experiment including the number of extractions as well as the choice of solvent and resin used to represent the class of polymer listed in this notification. In the notifier's 12/11/2009 response to our question as to whether the 95% ethanol study was truly exhaustive, the notifier points out that the second extraction was equivalent to 50% of the first and that the amounts that could reasonably be expected to be extracted in subsequent extractions (third and subsequent) would be minuscule. The notifier provides the following example, if a third extraction was conducted, the result would much lower than 50% of the first extraction. However, even if the third extraction is equivalent to 50% of the first extraction (0.060 mg/g) and adding this value to the value form the first (0.122 mg/g) and second (0.060 mg/g) extraction results, the total would be 0.242 mg/g, or 242 parts per million (ppm) oligomers. We agree with the notifier's approach to resolving this issue.

With respect to our question as to whether resin (b) (4) represents a worst-case for oligomer migration to food, the notifier points out that (b) (4) has the highest melt flow rate and, consequently, the lowest molecular weight of the resins listed in the notification. Therefore, it would represent a worst-case scenario for the migration of oligomers from resins covered by this submission.

Residual hexafluoropropylene, tetrafluoroethene, and perfluoroethylvinyl ether

The notifier analyzed representative samples of the FCS for residual monomers hexafluoropropylene (HFP), tetrafluoroethene (TFE), and perfluoroethylvinyl ether (PEVE) using headspace analysis/gas chromatography coupled with single ion monitoring mass spectrometry. Calibration curves ranging in concentration from 0.5- to 25 ppm were generated for each of the monomers. Correlation coefficients for each of the monomers calibration curves ranged from 0.9961 to 0.9968. The notifier subjected 10 grams of the polymer in a headspace vial to one hour in an oven at 180 ºC and then analyzed the headspace gasses for the monomers. In our deficiency letter, we questioned whether 180 °C for 1 hour is sufficient to characterize the residuals. In response, they stated that they do not "believe" a higher temperature or longer time would make any difference.

Although the boiling points of these materials are very low, even low-boiling materials can be entrapped within a polymer matrix and may not diffuse through the polymer under the testing conditions. As described by Jacobsson and Hagman,[1] it can take several hours or days to equilibrate the analyte between the gas phase and the solid phase. Once equilibrated, the headspace may be sampled and the concentration of the analyte determined in the headspace. As the gaseous material should be in equilibrium with the material in the solid phase, the concentration of the analyte in the headspace is only ½ of the total quantity of analyte that was originally in the sample before heating. Therefore, any measured quantity of analyte must be doubled to provide its concentration in the polymer. If the method is meant to be exhaustive, the sample must be heated multiple times at the appropriate time and temperature until no more of the analyte is detected.

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1 S. Jacobsson and A. Hagman, Drug Development and Industrial Pharmacy 1990, 16(17), 2547.

Given that most of the measurements were below the limit of detection, the conservative method for calculating exposure (100% migration of residue level), and the substitutional nature of the material, we will use the data provided, as well as applying a conservatism (2× their reported residual levels) in our exposure calculations. The notifier did not detect tetrafluoroethene above the stated limit of detection of 0.001 ppm in the resin. Hexafluoropropylene and perfluoroethylvinyl ether were detected in some of the representative samples of the resin. The average concentration of hexafluoropropylene in the samples was 0.0175 ppm and the average concentration of perfluoroethylvinyl ether in the resin samples was 0.001 ppm. As stated above, we will double these values to 0.002 ppm and 0.035 ppm.

(b) (4)

In their original submission, the notifier did not provide sufficient data to estimate exposure to (b) (4) or the decomposition product of (b) (4) (b) (4) and the decomposition product of have boiling points of approximately 55 °C and 144 °C, respectively. The notifier states that these materials are sufficiently volatile that they will not be present in the finished FCS after the numerous heating steps used in the production of these materials. The notifier pointed out that (b) (4) is also called (b) (4) which is mentioned in (b) (4) (b) (4) see Attachment 3 of the notification.

The notifier argued that (b) (4) (b.p. = 55 °C) is effectively removed from the FCS during processing and finishing. We agree with their conclusion for (b) (4) since it is used in post-polymerization processing and is not expected to become entrapped in the polymer matrix during synthesis and would, therefore, volatilize completely under the stated conditions. However, (b) (4) uses (b) (4) in the polymerization of (b) (4) and it could become entrapped in the polymer matrix. A similar situation is seen with polymers (b) and (b) as they contain quantifiable residual levels of (b) (4) which has a lower boiling point than (b) (4)

If any (b) (4) remained in the finished resins, it should migrate from the polymer to 95% ethanol along with any oligomers. Therefore, we can use the quantity of oligomers that migrate from these resins to food as a conservative estimate of the migration of (b) (4) to food. In the notifier's 12/11/2009 update to the notification, they provided an exposure estimate to (b) (4) based on the 95% ethanol extraction results for resin (b) (this resin was evaluated in FCN 948). As we have already accepted that the migration values from the (b) resin (242 ppm) are a worst-case scenario for the resins covered by this notification, we will use this value in our exposure estimates in place of those from the (b) resin.

The notifier analyzed representative samples of the FCS for (b) using LC/MS/MS and provided results of these analyses in Attachment 5 of the notification. However, they did not provide the appropriate supporting data, including raw data, calibration curves and supporting raw data, and validation studies and appropriate supporting data. These data were provided in Attachment 2 of the 12/31/2009 update to the

notification.[2] The analytical method used for these analyses was published in The Analyst.[3] The notifier analyzed, in duplicate, multiple batches of each of the four grades of the FCS for (b) The notifier prepared ten standards ranging in concentration from 0.1 to 150 ppb (b) (correlation coefficient of 0.9995). The quantity of (b) in the FCS ranged from below the limit of detection (0.02 ppm) to 4.97 ppm in the finished resin.[4] The analytical method was validated using an internal standard for each of the analyses.

(b) (4)

The notifier analyzed the finished FCS for residual (b) (4) using two separate methods, (b) chromatography and (b) (4) . Details of these analyses are presented in Attachment 6 of the notification. In both cases, the notifier extracted cryo-ground pellets of the FCS for 24-48 hours with refluxing deionized water. The maximum quantity of (b) (4) found in the water extracts was 15 ppm.

(b) (4)

As stipulated in Attachment 3 of the notification, the initiator (b) (4) (b) (4) and initiate polymerization or be converted into (b) (4) Given the high boiling point of (b) (4) , we would expect to see residuals of this material in the finished polymer. As such, the notifier provided the following worst-case estimate for the quantity of (b) (4) in the finished resin based on the maximum use level for (b) (4) n the resin, 1000 parts per million (ppm). Thus, the maximum level of potential migration, assuming 100% of the (b) (4) is converted to (b) (4) and 100% of the (b) (4) migrates to food, is calculated using the density of the FCS (2.14 g/cm^3), the thickness of the FCS (15 mil)[5], the quantity of (b) (4) used during manufacture (1000 ppm), and the total mass of food that will contact th cookware over its useful lifetime (2 x 10^4 g/in^2).

$$[(2.14\ g\ FCS/cm^3\ FCS)\ (16.4\ cm^3/in^3)\ (0.015\ in\ thick\ coating)/(2 \times 10^4\ g\ food/in^2\ bake\ ware)$$
$$(1000\ mg\ (b)\ (4)\ 1000g\ FCS)(1000\ g\ food/1\ kg\ food)] =$$

$$2.6 \times 10^{-5}\ mg\ (b)\ (4)\ /g\ food\ or\ 26\ \mu g\ (b)\ (4)\ /kg\ food$$

Exposure Estimates

The notifier provided the following examples of articles to be manufactured from the FCS: 1) tubing having a diameter of 0.25-10 inches, and expected useful life of 5-10 years, 2) coatings on metal bake ware/cookware for cooking applications, and 3) coatings on metal pipe linings. The maximum thickness of the FCS when used as a coating will be 15 mils. The notifier developed two exposure scenarios for the use of their FCS. Although the notifier provided

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2 The notifier only provided supporting data for the measurement of (b) (4) in resin type D as it was determined to contain the highest level of this substance in the FCS. Therefore, we will consider this data representative of the four resin types presented in this notification.

(b) (4)

4 The notifier used a value of 0.42 ppm as the highest quantity of (b) detected in the FCS, however, table 2 of Attachment 5 indicates that an A type resin contained 4.97 ppm (b) We will use 4.97 ppm in our exposure estimates as it is the highest value reported for the four types of resin presented in this FCN.

5 The notifier used a thickness of 10 mils in their calculations. We will use a thickness of 15 mils as this is the thickness stipulated on page 9 of Form 3480.

other use examples, these two scenarios are generally representative of the range of intended uses.

Cookware

A representative size cookware container is one that has dimensions of 3 inches in height, 8 inches wide, and 10 inches long. When filled within 0.25 inch of the top, the volume is calculated to be 2.75 in x 8 in x 10 in = 220 in^3 = 3608 cm^3 = 3608 g food (assuming a density of 1 g/cm^3); the internal food-contact surface area is calculated to be approximately 179 in^2. Thus, the food mass-to-surface area ratio for each use would be (3608 g)/(179 in^2) = 20 g/in^2. Therefore, a typical amount of food contacted over the service life of the article is expected to be approximately 1000 uses x 20 g/in^2 = 2.0 x 10^4 g food/in^2.

Pipe Linings

The pipes will have approximate diameters of 2-4 inches with a length of 20- 40 feet; some pipes may have diameters of up to 8 inches with lengths of up to 100 feet. The flow rate in a 6-inch diameter pipe will be approximately 150 million pounds per year. The coatings are expected to have a useful life of 5-10 years. The 6 inch pipe is employed as a useful representative to calculate the food-to-surface area ratio. The circumference of a 6 inch circle is 18.9 in, and the surface area of a 100 foot length is (18.9 in) x (100 ft) x (12 in/ft) = 22,680 in^2. Over the minimum expected lifetime, the total amount of food would be (150 x 10^6 lb/year) x (454 g/lb) x (5 years) = 3.41 x 10^{11} g. Therefore, the food mass-to-surface area ratio over the lifetime is (3.41 x 10^{11} g) / (22,680 in^2) = 1.5 x 10^7 g/in^2.

The first repeated-use scenario provides the most conservative estimate for the quantity of food in contact with the FCS of 2 x $10^4 g/in^2$. We will use this value in our exposure estimates.

Oligomers

Using our default consumption factor for new polymers (0.05),[6] the density of the FCS (2.14 g/cm^3), a thickness of 15 mils, the oligomer level of 242 ppm, the quantity of food contacting cookware coated with the FCS (2 x $10^4 g/in^2$) and the assumption of 100% migration of the oligomers to food, the dietary concentration (DC) of oligomers is calculated as follows.

$$DC = [(0.05)(2.14\ g\ FCS/cm^3\ FCS)(0.015\ in\ thick)(16.4\ cm^3/in^3)(242\ mg\ olig./1000\ g\ FCS)/(2 \times 10^4 g/in^2)] =$$

$$3 \times 10^{-7}\ mg\ oligomers/g\ food\ or\ 0.3\ ppb$$

The estimated daily intake (EDI) of the oligomers is calculated by multiplying the DC of 0.3 ppb by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = 0.3\ ppb \times 3\ kg/p/d = 0.9\ \mu g/p/d$$

6 Rather than using a typical repeat-use scenario, K&H used our minimum consumption factor of 0.05, which we feel is appropriately conservative for these uses. This is consistent with the method used to calculate exposure to a very similar resin covered by FCN 948.

Hexafluoropropylene, tetrafluoroethene, and perfluoroethylvinyl ether

As calculated above, the average concentrations of hexafluoropropylene, tetrafluoroethene, and perfluoroethylvinyl ether are 0.035 ppm, 0.002 ppm, and 0.002 ppm, respectively. The DCs and EDIs of these monomers are calculated in the same fashion as the oligomers. A sample calculation for hexafluoropropylene is shown below.

$$DC= [(0.05)(2.14 \text{ g FCS/cm}^3 \text{ FCS})(0.015 \text{ in})(16.4 \text{ cm}^3/\text{in}^3)(0.035 \text{ mg}/1000 \text{ g FCS})/ (2 \times 10^4 \text{g/in}^2)] =$$

$$4.6 \times 10^{-11} \text{ mg oligomers/g food or } 4.6 \times 10^{-5} \text{ ppb}$$

The estimated daily intake of the oligomers is calculated by multiplying the DC of 4.6×10^{-5} ppb by our standard assumption that a person consumes 3 kg of food per day.

$$EDI = 4.6 \times 10^{-5} \text{ ppb} \times 3 \text{ kg/p/d} = 1 \times 10^{-4} \text{ µg/p/d}$$

(b) (4) are expected to decompose to (b) (4) during polymerization and purification.[7] Therefore, there will be no exposure to (b) (4). The breakdown products (b) (4) are affirmed as GRAS for direct addition to food under (b) (4) and (b) (4) and would be removed during purification; exposure to this material would be essentially zero.

(b) (4) gasses and are expected to volatilize from the FCS during purification and sparging. (b) (4) will also be removed during purification. Therefore, exposure to (b) (4) will be essentially zero.

(b) (4)

As stated above, we will use the migration value from the (b) (4) resin (242 ppm) as a worst-case value of estimating exposure to (b) (4). Using the equations provided above, we estimate the DC and EDI of (b) (4) to be 0.3 ppb and 1 µg/p/d, respectively.

(b) (4) Given the above finishing steps, we estimate that the DC of (b) (4) would be much lower than the 0.3 ppb calculated above.

(b) (4) is regulated in (b) (4) (Emulsifiers and/or surface-active agents) for use in the production of food contact materials.

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7 A review of the FAPs that lead to 177.1550 ((Perfluorocarbon resins)) revealed that (b) (4)

(b) (4)

The quantity of (b) (4) in the FCS ranged from below the limit of detection (0.02 ppm) to 4.97 ppm in the finished resin. Using the equations for calculating the DC and EDI shown above and the maximum residual level of (b) (4) (4.97 ppm), gives a DC and EDI of 0.0065 ppb and 0.02 µg/p/d, respectively.

(b) (4)

Using the equations for calculating the DC and EDI shown above and the maximum residual level of (b) (4) (15 ppm), we have estimated a DC and EDI of (b) (4) to be 0.02 ppb and 0.06 µg/p/d, respectively.

(b) (4)

Using the maximum quantity of (b) (4) that could migrate to food (26 µg/kg food) and a consumption factor of 0.05, the DC of (b) (4) is 1.3 ppb. The EDI is 4 µg/p/d. Although the material has a high boiling point (144 °C) we would expect some of the (b) (4) to be removed during processing and purification. Given that some of the (b) (4) is likely removed during purification and the fact that we assumed 100% of the initiator was converted to (b) (4) and that 100% of this amount migrated to food, the 1 ppb DC for (b) (4) is conservative exposure estimate for this material. In actuality, we expect the DC for this material to be much less than 1 ppb, but we are unable to refine the exposure estimate due to the lack of data.

(b) (4)
(b) (4) is affirmed as GRAS for direct addition to food under (b) (4)
(b) (4)).

Tentative Exposure Estimates

Compound	DC (ppb)	EDI (µg/p/d)
FCS oligomers	0.32	1
Tetrafluoroethylene	2.6×10^{-6}	8×10^{-6}
Hexafluoropropylene	4.6×10^{-5}	1×10^{-4}
Perfluoroethylvinyl ether	2.6×10^{-6}	8×10^{-6}
(b) (4)	GRAS	(b) (4)
	GRAS	
	Essentially	
	Essentially	Zero
	0.32	1
	Regulated	(b) (4)
	0.0065	0.02
	0.019	0.06
	Essentially	Zero
	1.3	4
	Essentially	Zero
	GRAS	(b) (4)

Cumulative Estimated Daily Intake (CEDI)

The FCS is a new resin and therefore the EDI for the oligomers is the current CEDI for this material. As for (b) (4) there will be no increase in its CEDI as the uses are substitutional for those currently regulated.

Conditions of use J Restrictions

As exposure to conditions of use J were evaluated on the basis of 100% migration, no limitations other than the functionality of the polymer need be imposed.

Kirk Arvidson, Ph.D.

HFS-275 (Chemistry Reading File)
HFS-275: KBArvidson:436-1152:FCN000947_C_MEMO: 3/15/2010
R/D Init: MAAdams:3/19/2010
Final: kba:3/22/2010

Cumulative Estimated Daily Intake (CEDI)

The FCS is a new resin and therefore the EDI for the oligomers is the current CEDI for this material. As for (b) (4) [redacted], there will be no increase in its CEDI as the uses are substitutional for those currently regulated.

Conditions of use J Restrictions

As exposure to conditions of use J were evaluated on the basis of 100% migration, no limitations other than the functionality of the polymer need be imposed.

(b) (4), (b) (6) [redacted]

Kirk Arvidson, Ph.D.

HFS-275 (Chemistry Reading File)
HFS-275: KBArvidson:436-1152:FCN000947_C_MEMO: 3/15/2010
R/D Init: MAAdams:3/19/2010
Final: kba:3/22/2010

CHEMOURS FCN 948

FOR USE IN REPEAT-USE
FOOD CONTACT ARTICLES

Part II - CHEMISTRY INFORMATION

SECTION A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE

See Chemistry Recommendations, Sections II.A.1 through 4.

1. Chemical Abstracts Service (CAS) name

Ethene, 1,1,2,2-tetrafluoro-, polymer with 1,1,2-trifluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethene

2. CAS Registry Number

31784-04-0

3. Trade or Common Name

PFA polymer; tetrafluoroethylene-perfluoro(ethyl vinyl ether) copolymer

4. Other Chemical Names *(IUPAC, etc.)*

5. Description

Provide a description of the FCS, including chemical formula(s), structure(s) and molecular weight(s). For FCSs that cannot be represented by a discrete chemical structure, such as new polymers, provide a representative chemical structure(s) and the M_w and M_n. For new copolymers, also provide the ratio of monomer units in the copolymer.

The different polymer "grades" have different specifications, and A and B represent different manufacturing processes. The following are representative grades:

Polymer "Grades"	Perfluoroethyl vinyl ether (PEVE) (%)	Tetrafluoroethylene (TFE)
Manufacturing Process A		
(b) (4) [redacted]		

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

6. Characterization

Attach data, such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), mass spectra, or other similar data for identification of the FCS.

See FTIR spectra in **Attachment 1**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B - MANUFACTURE

See Chemistry Recommendations, Sections II.A.4.a through d.

1. List all reagents monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS. Include chemical name, CAS Reg. No., and function in the manufacture of the FCS.

CHEMICAL NAME	CAS REG. NO.	FUNCTION	Is residual expected to remain in the final food contact material?†
Tetrafluoroethylene (TFE)	116-14-3	Monomer	☒ Yes ☐ No
Perfluoroethylvinyl ether (PEVE)	10493-43-3	Monomer	☒ Yes ☐ No
(b) (4)			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☒ Yes ☐ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☒ No
			☐ Yes ☐ No
			☐ Yes ☐ No
			☐ Yes ☐ No

† If yes, include in Table II.B.3. If no support this conclusion in the manufacturing process description (#2).

2. Describe the manufacturing process, including reaction conditions (e.g., times and temperatures), and include chemical equations and stoichiometry for all synthetic steps and side reactions. Describe any purification steps.

See manufacturing process descriptions and lists of process ingredients in **Attachment 2**.

Also included with this attachment is a description of processing steps which may occur when the materials of interest are used in a particular application – in this case, a coatings application. This level of detail is included to help more fully describe the complete process sequence the materials may experience in this type of unique application.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION B – MANUFACTURE *(continued)*
See Chemistry Recommendations, Sections II.A.4.a through d.

3. List impurities in the FCS including: the chemical names, CAS Reg. Nos., and typical and maximum residual levels (percent weight) in the FCS as it will be marketed. For FCSs that are polymers, include typical and maximum residual monomer concentrations. Provide supporting data including analytical methods and validation information.

CHEMICAL NAME	CAS REG. NO.	TYPICAL RESIDUAL (%)	MAXIMUM RESIDUAL (%)	Is residual expected to migrate from the final food contact material?†
Tetrafluoroethylene (TFE)	116-14-3	<0.001 ppm	-	☒ Yes ☐ No
Perfluoroethylvinyl ether (PEVE)	10493-43-3	0.001-3.1 ppm	-	☒ Yes ☐ No
(b) (4)		0.02-4.97 ppm	-	☒ Yes ☐ No
		5.37-7.38 ppm	-	☒ Yes ☐ No
			-	☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No
				☐ Yes ☐ No

† If yes, ensure that exposures to these substances are addressed in Section II.G of this form. If no, provide an explanation below.

See **Attachment 3** for residual monomer report.

See **Attachment 4** for residual (b) report.

See **Attachment 5** for extractable (b) (4) analysis report.

See **Attachment 12** for discussion regarding the expected absence of (b) (4) in the FCS.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS
See Chemistry Recommendations, Section II.A.5 and 6

Provide physical and chemical specifications for the FCS such as density, melting point, maximum impurity levels, and solubility in food simulants. Provide specification test results for at least three production batches of the FCS and attach methods for establishing compliance with specifications. For Values, provide minimum or maximum specification limits or a range, as appropriate.

1. For the FCS:

SPECIFICATION	VALUE
See Attachment 6	

2. For polymeric FCSs provide the following additional information:

a. Polymer Properties and Test Results of Production Batches

Provide relevant physical data, such as molecular weight distr bution, glass transition points, intrinsic or relative viscosities, melt flow indices, morphology, and crystallinity. Analytical methods should be included. Where appropriate, provide test results for at least three production batches of the FCS. **See Attachment 7 for specification test methods.**

PROPERTY	MAX. VALUE	MIN. VALUE	INDIVIDUAL BATCH VALUES
See Attachment 6			

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION C – PHYSICAL/CHEMICAL SPECIFICATIONS *(continued)*

b. Molecular Weight Profile of the FCS

Provide a value for the maximum percentage of oligomeric species (not including residual monomers, reactants, or solvents) below 1000 Daltons and include supporting data and analytical methods.

The molecular weight distribution of the FCS cannot be determined, as the polymer is not soluble in any solvents in which molecular weight determination can be performed. Thus, the molecular weight distribution is not known.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION D - INTENDED USE

See Chemistry Recommendations, Sections II.B and II.C

1. Describe the intended use of the FCS. Include maximum use level(s) in food-contact materials, types of food-contact articles with or in which the FCS is expected to be used (e.g., films, coatings, molded articles) and maximum thickness, as applicable. Indicate whether single or repeat use (or both) is intended: ☐ Single Use ☒ Repeat Use

The food-contact substance (FCS) will be used in repeated-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings. The coatings will have a maximum thickness of 15 mils.

Proposed language for listing on FDA's "Inventory of Effective Food Contact Substance Notifications" website is provided in **Attachment 9**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. a. For single-use articles, list the food types expected to contact the FCS, with examples if known. Refer to the food type classifications in the chemistry recommendations, when possible. Also provide maximum temperatures and times of food contact, referring to the conditions of use in the chemistry recommendations, when possible. *(click here for example)*

USE	FOOD TYPE	CONDITION OF USE

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION D - INTENDED USE *(continued)*

2. a. CONTINUED

USE	FOOD TYPE	CONDITION OF USE

b. For repeat-use articles, provide a typical use scenario. Include the highest intended use temperature, maximum food-contact time for the article, and typical amount of food contacted over the service lifetime of the article.

The FCS will be used in repeated-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings. The FCS will contact all food types under Conditions of Use A through H, and J.

As an example of articles, tubing may have a diameter of 0.25 – 10 inches, and is expected to have a useful life of 5 – 10 years. With regard to coatings, they will have a maximum thickness of 15 mils and may be comprised entirely of the FCS. The coatings may be used on metal bakeware or cookware for cooking applications, and for coatings on metal pipe linings. We have developed representative use scenarios for bakeware and pipes.

A representative size bakeware/cookware container has dimensions of 3 inches in height, 8 inches wide, and 10 inches long. When filled within 0.25 inch of the top, the volume is calculated to be 2.75 in x 8 in x 10 in = 220 in^3 = 3608 cm^3 = 3608 g food (assuming a density of 1 g/cm^3); the internal food-contact surface area is calculated to be approximately 179 in^2. Thus, the food mass-to-surface area ratio for each use would be (3608 g) ÷ (179 in^2) = 20 g/in^2. Therefore, a typical amount of food contacted over the service life of the article is expected to be approximately 1000 x 20 g/in^2 = 2.0 x 10^4 g food/in^2.

The pipes will have approximate diameters of 2 – 4 inches with a length of 20 – 40 feet; some pipes may have diameters of up to 8 inches with lengths of up to 100 feet. The flow rate in a 6-inch diameter pipe will be approximately 150 million pounds per year. The coatings are expected to have a useful life of 5 – 10 years. The 6 inch pipe is employed as a useful representative to calculate the food-to-surface area ratio. The circumference of a 6 inch circle is 18.9 in, and the surface area of a 100 foot length is (18.9 in) x (100 ft) x (12 in/ft) = 22,680 in^2. Over the minimum expected lifetime, the total amount of food would be (150 x 10^6 lb/year) x (454 g/lb) x (5 years) = 3.41 x 10^{11} g. Therefore, the food mass-to-surface area ratio over the lifetime is (3.41 x 10^{11} g) ÷ (22,680 in^2) = 1.5 x 10^7 g/in^2.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

3. State the intended technical effect of the FCS. Summarize data demonstrating that the FCS will achieve the intended technical effect. Specifically address the minimum amount required to achieve the intended technical effect. Include data as an attachment.

   See **Attachment 10** for representative product information sheets.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

SECTION E - STABILITY DATA

See Chemistry Recommendations, Section II.D.2

1. Describe any degradation, decomposition or other chemical breakdown process (oxidation, photolysis, hydrolysis, etc.) that the FCS may undergo during either its intended use in the manufacture of a food-contact article or during migration testing (if performed) of a test plaque containing the FCS. If no degradation is expected, so state.

   No degradation is expected. See Thermogravimetric Analysis (TgA) data in **Attachment 11**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION

2. List the breakdown products for the FCS and provide CAS names, CAS Reg. Nos., and structures, as appropriate. Address the amount of any breakdown products that migrate to food and ensure that exposures to these substances are addressed in Section II.G of this form.

SUBSTANCE NAME	CAS REG. NO.	SUBSTANCE NAME	CAS REG. NO.
STRUCTURE		**STRUCTURE**	
SUBSTANCE NAME	**CAS REG. NO.**	**SUBSTANCE NAME**	**CAS REG. NO.**
STRUCTURE		**STRUCTURE**	

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD

See Chemistry Recommendations, Sections II.D and Appendix II

Summarize information on migration testing and/or calculations in the appropriate sections below for both the FCS and any migrants. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached.

If exposure estimates are determined by assuming 100% migration to food, or through the use of other methods *(see Chemistry Recommendations II.D.5)*, skip to Section II.F.2 and provide full details of all calculations.

For repeat-use articles, estimate migrant levels in food using migration testing and/or calculations which take into account the amount of food contacting the article over its service lifetime *(see Chemistry Recommendations, Appendix II, Part 4)*.

1. MIGRATION TESTING OPTION

See Chemistry Recommendations, Sections II.D.1 through II.D. 3

a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants, levels of residual monomer(s)), dimensions (thickness and surface area), and relevant base polymer properties (e.g., density, T_g, T_m, % crystallinity). Indicate whether specimens were extracted by total immersion or exposed to solvent on a single side.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

b. Identify food or food simulants employed, times and temperatures of extraction, volume of simulant used per extraction, and food stimulant volume-to-specimen surface area ratio (e.g., 10% ethanol, conditions of use A [121°C/2 h, then 40°C/238 h], 200 mL of 10% ethanol solution per extraction, 10 mL/in²). If the food simulant volume-to-specimen surface area ratio is less than 10 mL/in², provide evidence (e.g., turbidity or precipitation data) showing that saturation of the food simulant has not occurred.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

c. Summarize results of migration testing for each test specimen. Give individual and average migration values (mg/in²) for all analytes in each simulant at all time points (an example of how the data should be presented is given below). In addition, provide sample calculations relating the instrumental output to reported migration values in mg/in². For new polymers, provide a measure of oligomer migration and, if possible, characterize the individual low-molecular weight oligomer components. *(click here for example)*

SUMMARY OF MIGRATION TESTING

TEST SAMPLE FORMULATION	MIGRANT	FOOD OR FOOD SIMULANT	TEMPERATURE AND TIME OF ANALYSIS	MIGRATION *(each replicate)*	AVERAGE MIGRATION *(average of replicates)*
Not applicable.					

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION F - MIGRATION LEVELS IN FOOD *(continued)*

d. Provide a summary of method validation results. Give average percent recovery for all analytes, food or food simulants, and fortification (spiking) levels. Full details, including description of sp king procedure and calculations, must be included as an attachment.

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. MIGRATION CALCULATION OPTION

See Chemistry Recommendations, Sections II.D. for discussions on 100% migration calculations, II.D.4 for information on FDA's migration database, and II.D.5 for migration modeling.

Describe the basis of the mathematical approach used in estimating migration levels to food for the FCS or any migrants, such as impurities, monomers or breakdown products, in the FCS. Fully descr be assumptions made in deriving the estimates and show all calculations.

See migration calculations in **Attachment 12**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI)

See Chemistry Recommendations, Sections II.E and Appendix IV

The EDI for the notified use must be calculated by the notifier for both the FCS and any migrants. The notifier is also responsible for providing cumulative EDIs (CEDIs) reflecting any previously regulated, notified, or otherwise authorized uses of the FCS. The notifier may wish to consult FDA to obtain this information prior to submitting a notification.

1. SINGLE-USE ARTICLES

Show representative calculations for the EDI for all migrants. Clearly descr be the food-type distribution factors (f_T) and consumption factors (CF) used in the calculations *(see Chemistry Recommendations Appendix IV)*. If f_T and/or CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached. The following general equation is used to calculate an EDI:

EDI = DC x 3 kg food/p/d
= CF x <M> x 3 kg food/p/d
= CF x $[(M_{aq})(f_{aq})+(M_{ac})(f_{ac})+(M_{al})(f_{al})+(M_{fat})(f_{fat})]$ x 3 kg/p/d

where: (aq) is aqueous, (ac) is acidic, (al) is alcoholic, and (fat) is fatty

Not applicable.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

2. REPEAT-USE ARTICLES

Using the migration levels to food determined in Section II.F.2 and the use scenario information descr bed in Section II.D.2.b, show the calculations used for determining DC and EDI for the FCS and any migrants.

See dietary exposure calculations in **Attachment 13**.

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number in Section VI of this form.

Part II - CHEMISTRY INFORMATION *(continued)*

SECTION G - ESTIMATED DAILY INTAKE (EDI) *(continued)*
See Chemistry Recommendations, Sections II.E and Appendix IV

3. SUMMARY OF THE CHEMISTRY INFORMATION

Summarize the values for weight-average migration (<M>), dietary concentration (DC), and EDI for the FCS and any migrants, including oligomeric species and breakdown products, as appropriate. Provide cumulative EDI (CEDI) to include this use, where appropriate.

CHEMICAL NAME	CAS REG. NO.	<M> (ppb)	DC (ppb)	EDI (mg/person/day)	CDC (ppb)
Oligomers	31784-04-0	9.0	0.45	0.00135	0.45
Tetrafluoroethylene (TFE)	116-14-3	0.000018	0.0000009	2.7×10^{-9}	-
Perfluoroethylvinyl ether (PEVE)	10493-43-3	0.054	0.0027	8.1×10^{-6}	-
(b) (4) [redacted]		0.087	0.0044	1.3×10^{-5}	-
		0.13	0.0065	2.0×10^{-5}	-

Memorandum

Date: January 22, 2010

From: Division of Food Contact Notifications
Chemistry Team 2

Subject: FCN #948: Review of a submission received 10-27-09 from Keller and Heckman on behalf of E.I. du Pont de Nemours and Company. Ethene, 1,1,2,2-tetrafluoro-, polymer with 1,l,2-trifluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethene in repeat-use food-contact articles.

To: Division of Food Contact Notifications
Regulatory Team 1
Attn: M. Hepp, Ph.D.

Keller and Heckman (K&H), on behalf of E. I. du Pont de Nemours and Company (DuPont), have submitted this Food-Contact Notification (FCN) for the food-contact substance (FCS): Ethene, 1,1,2,2-tetrafluoro-, polymer with 1,l,2-trifluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethene (CAS# 31784-04-0) in repeat-use food-contact articles. The FCS may contact all food types under Conditions of Use A through H, and J, as described on our website.[1]

The FCS will be used in repeat-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings.

Background

This is a new food-contact polymer. There are no current listings either as a regulated material (21 *CFR* 177.1550, Perfluorocarbon resins), or as an effective notification.

The copolymer is made from tetrafluoroethylene (TFE) and perfluoro(ethyl vinyl ether) (PEVE). [redacted][2]

Identity

CAS Name: Ethene, 1,1,2,2-tetrafluoro-, polymer with 1,l,2-trifluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethene

Trade Name: PFA Polymer
Tetrafluoroethylene-perfluoro(ethyl vinyl ether) copolymer

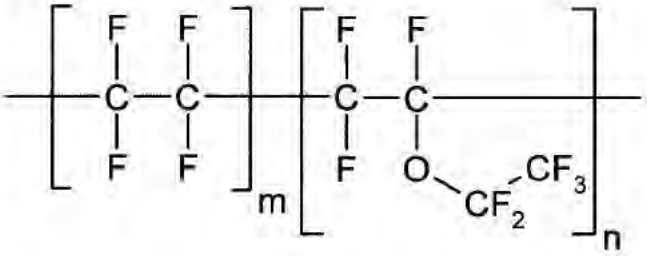
[1] http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/ucm081818.htm#av2.

[2] Resulting from [redacted]

CAS Reg. No.: 31784-04-0

Molecular Weight: Not measurable[3]

Structure:



Based on the grades listed (about 8% PEVE),[4] m is about 25 and n is about 1.

The submission includes a Fourier-transform infrared spectrum (FTIR) consistent with the proposed structure (Attachment 1).

We have no questions regarding the identity of the FCS.

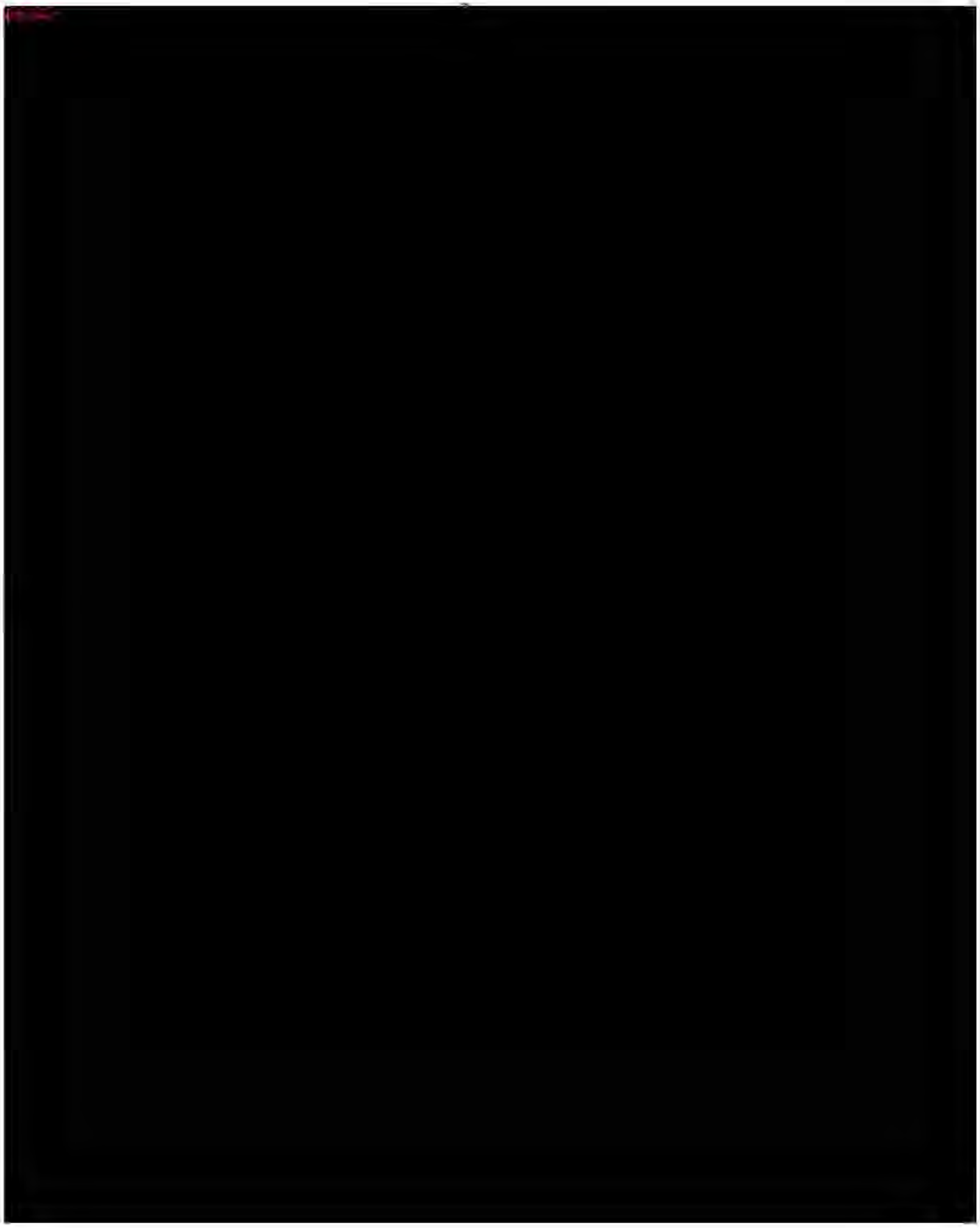
Manufacture

(b)(4)

[redacted]

[3] K&H state the molecular weight distribution of the FCS cannot be determined, as the polymer is not soluble in any solvents in which molecular weight determination can be performed.

[4] FAP 9B3459 described a copolymer of 96% TFE and 4% PPVE.



Intended Technical Effect and Use Level

The FCS will be used in repeat-use food-contact applications, such as articles (tubing, tanks, and fittings for food equipment), coatings on metal bakeware and cookware, and coatings on metal pipe linings. The coatings will have a maximum thickness of 15 mils.

DuPont has included product information (Attachment 10) stating this resin is similar to the regulated TFE/PPVE copolymer with the additional benefits of improved flex life and chemical stress crack resistance. The FCS would function as a non-stick coating.

Stability

DuPont has included thermogravimetric analysis (TGA) of the FCS (Attachment 11). Samples were heated to 177°C (350 °F) in air and held for 120 minutes. Although the curves are somewhat noisy, there is no indication of any degradation at the test temperature. In your deficiency letter (11-18-09, M. Hepp to G. Misko), you passed on our request for thermogravimetric data (TgA) demonstrating the stability of the polymer at temperatures of up to 230°C (typical frying temperature). DuPont has now generated the TgA data (response from G. Misko to M. Hepp, 12-7-09) at that temperature for several grades of the polymer (Attachment 1). While it is not the type of scan we had anticipated (polymer weight as a function of temperature), it does show stability and, given the low exposures expected from these repeat uses, it is acceptable.

Migration Studies

No migration studies were performed. K&H have based exposure estimates on residual levels in the polymer and repeat-use of the FCS. Typical repeat-use scenarios are described in Form 3480(II)(D)(2)(b).

K&H have estimated exposure based on an assumption of 100% migration of the components of the polymer to food. In performing these calculations, it has been assumed that the portion of the food-contact article that will potentially contribute the substances is the 10 mil (0.01 inch) thick layer in contact with the food. This is not consistent with the stated maximum thickness of 15 mil.

In addition, they have used what they refer to as "exhaustive" extraction of samples using hexane and 95% ethanol (EtOH) in a Soxhlet extractor for 24 hours, followed by an additional 24 hours using fresh solvent (Attachment 8). We did not concur that this is truly exhaustive, since the second extraction using hexane actually produces more extractives than the first, and the second EtOH extraction is fully 20% of the first sample. You asked about this point in your deficiency letter, and their response included a discussion of a possible third extraction giving a total of 606 ppm of extractives (compared with 517 ppm in the initial estimate). We find this to be suitably conservative.

Attachment 3 is a report of headspace gas chromatography being used to measure residual monomers in the FCS. We questioned whether 180°C for 1 hour is sufficient to characterize the residuals. In response, they again say they do not "believe" a higher temperature or longer time would make any difference.

Exposure estimates should be supported by data, not based on faith. As was noted in the deficiency letter for FCN 947 (for a very similar FCS, E. Furukawa to G. Misko, 12-22-09), although the boiling points of these materials are very low, even low boiling materials can be entrapped within a polymer matrix and may not diffuse through the polymer under the given set of testing conditions. As described by Jacobsson and Hagman,[6] it can take several hours or days to equilibrate the analyte between the gas phase and the solid phase. Once equilibrated, the headspace may be sampled and the concentration of the analyte determined in the headspace. As the gaseous material should be in equilibrium with the material in the solid phase, the concentration of the analyte in the headspace is only ½ of the total quantity of analyte that was originally in the sample before heating. Therefore, any measured quantity of analyte must be doubled to provide its concentration in the polymer. If the method is meant to be exhaustive, the sample must be heated multiple times at the appropriate time and temperature until no more of the analyte is detected.

However, given the low exposure to the FCS and the substitutional nature of the material, we will use the data provided, as well as applying a conservatism (2× their reported residual levels) in our exposure calculations. This will ensure that all exposure is accounted for.

Since K&H have based their exposure estimates on 100% migration of the measured levels of residuals from a 10 mil coating, and they are requesting a maximum coating thickness of 15 mil, we will adjust their estimates upward by 50%.

In summary, the reported residual levels and resulting migration would be:

Component	Level in FCS, ppm	Maximum Migration, ppb
Oligomers	606	15
TFE	0.002	0.000054
PEVE	6.2	0.16
(b) (4)	4.97	0.13
	7.38	0.20

Exposure

Rather than use a typical repeat-use scenario, K&H have used our minimum consumption factor (CF) of 0.05, which we feel is appropriately conservative for this rather specialized use. As an

[6] S. Jacobsson and A. Hagman Drug Development and Industrial Pharmacy 1990, 16(17), 2547.

example, for the oligomers, the dietary concentration (DC) would therefore be 0.05 times the migration potential, or:

$$DC = 0.05 \times 15 \text{ ppb} = 0.75 \text{ ppb}$$

and the resulting estimated daily intake (EDI), assuming a daily diet of 3000 grams of food per person per day, would be:

$$EDI = 0.75 \times 10^{-9} \text{ g oligomer/g food} \times 3000 \text{ g food/p/d} = 2.2 \times 10^{-6} \text{ g/p/d}$$

or 2.2 μg/p/d.

Similarly for the remaining potential migrants:

Component	CAS Reg. No.	DC (ppb)	EDI (μg/p/d)
Oligomers	-	0.75	2.2
TFE	116-14-3	0.0000027	0.0000081
PEVE	10493-43-3	0.008	0.024
(b) (4) [redacted]		0.0065	0.020
		0.01	0.03
		Essentially zero	-

Even though our estimates are 1.5 - 3× those determined by K&H, because of our added conservatisms on FCS thickness and headspace analysis, the exposures are still quite low.

We also note the discussion of (b) (4) [redacted], which is listed in the table of ingredients in the manufacture but is apparently not discussed in either the manufacturing process of the finishing steps. K&H pointed out that (b) (4) [redacted] is also called (b) (4) [redacted] which is mentioned in Process B (*Manufacture*, above). K&H argue (Attachment 12, p. 2) that this solvent (b.p. = 55°C) is effectively removed from the FCS during processing and finishing (DC = essentially zero). We agree with their conclusion. This is a separate issue from the residual monomer question, since it is used in post-polymerization processing and would not be expected to have become entrapped in the polymer matrix during synthesis and would, therefore, volatilize completely under the stated conditions.

Cumulative Estimated Daily Intake (cEDI)

These would be the cumulative exposures for the oligomers and PEVE. All of the other substances used in the manufacture are the same as for the currently regulated material. This

FCS would serve as a replacement for the regulated polymer and would not increase any exposures already determined from FAP 9B3459.[7]

Conclusion

We have no questions.

Michael C. VanDerveer, Ph.D.

HFS-275 (R/F)
HFS-275:MVanDerveer:(301)436-1254:FCN9248_C_Memo.wpd:mcv:01-07-10
R/DInit:HFS-275:MAAdams:1-22-10
F/T:mcv:1-22-10

[7] For example, the DC for (b)(4) [redacted]