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OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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SUBJECT: **Dimethoate:** Human Health Risk Assessment for Registration Review

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This document provides the HED's human health risk assessment for the Registration Review of dimethoate (*O,O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorodithioate). The hazard characterization, endpoint selection, and risk assessment were provided by Monique Perron (RAB1); the residue chemistry assessment was provided by George Kramer (RAB1), dietary exposure assessments were provided by Julie Van Alstine (RAB6); the occupational and residential exposure assessment was provided by Kelly Lowe and Jennifer Tyler (RAB1); and the drinking water assessment was provided by José Meléndez of the Environmental Fate and Effects Division (EFED).

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1.0 Executive Summary

Background

Dimethoate is a general use systemic, organophosphate (OP) insecticide/acaricide that is used to control a wide variety of insect pests. There are numerous end-use product labels registered with dimethoate as the active ingredient. These include liquid and water-soluble packets (WSP) formulations. The labeled use sites include various agricultural crops, Christmas tree farms, trees grown for pulp, and ornamentals in outdoor nurseries. Most of the registered products are applied via aerial, chemigation, airblast, groundboom, or with handheld equipment. For most use sites/crops, the maximum application rate is 2 lb ai/A, but for ornamentals in outdoor nurseries, the maximum application rate is 4.15 lb ai/A for airblast applications specifically. There are currently no registered or proposed residential uses of dimethoate.

Hazard Assessment

Dimethoate is a member of the OP class of pesticides. Like other OPs, the initiating event in the adverse-outcome pathway (AOP)/mode of action (MOA) for dimethoate involves inhibition of the enzyme acetylcholinesterase (AChE) via phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. For dimethoate, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. Dimethoate, like some other OPs, requires metabolic activation to its oxon metabolite (omethoate) to inhibit AChE, with subsequent metabolism that leads to detoxification. OPs also exhibit a phenomenon known as steady-state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. Therefore, a steady-state exposure assessments of 21 days and longer were conducted instead of the traditional chronic or long-term assessments.

The toxicology databases for dimethoate and omethoate are complete for risk assessment. There are acceptable studies available for toxicity endpoint selection. Dimethoate and omethoate have high-quality dose-response data across multiple lifestages, durations, and routes for both red blood cell (RBC) and brain AChE inhibition. High-quality dermal and inhalation studies allow for route-specific evaluation. Clinical signs of neurotoxicity can be found throughout the databases at doses much higher than those causing inhibition of AChE. No studies in the toxicology databases suggest quantitative sensitivity to dimethoate/omethoate based on AChE inhibition. Increased pup mortality was observed in several studies, but regulation of exposure to dimethoate and its oxon omethoate using brain AChE inhibition is protective of the observed pup mortality. For all exposure scenarios, interspecies (10X) and intraspecies (10X) uncertainty factors were applied. The Food Quality Protection Act (FQPA) Safety Factor (SF) has been retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). As a result, the FQPA SF was applied to all exposure scenarios except for dietary exposures for the adult population subgroup 50-99 years old, where the FQPA SF did not apply (total uncertainty factor = 100X).

Dimethoate is classified as a Group C carcinogen (possible human carcinogen). The Agency determined that quantification of risk using a non-linear approach would adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

Toxicity Adjustment Factors

As the oxon metabolite of dimethoate, omethoate has been found to be a more potent AChE inhibitor. To account for the increased potency of omethoate in risk estimates, benchmark dose (BMD) modeling was used to evaluate relative potency for dimethoate and omethoate and to estimate the toxicity adjustment factors (TAFs) for acute and steady-state exposure durations. The acute TAF from the Reregistration Eligibility Document (RED) for omethoate has been updated to 8X. The steady-state TAF of 3X for omethoate used in the RED was verified with additional data; therefore, no changes were made to the steady-state TAF.

Dietary (Food and Water) Exposure and Risk

Highly refined acute and steady-state dietary exposure and risk assessments for dimethoate and its metabolite omethoate were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.18. This model uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The steady-state dietary assessments provide a conservative estimate of 21-day average daily exposures using two-day average dietary exposure and 21-day rolling water averages. Acute and steady-state assessments were conducted for food only, drinking water only, and for food and drinking water.

The acute and steady-state dietary exposure assessments incorporated USDA Pesticide Data Program (PDP) data for dimethoate and omethoate, percent crop treated (PCT) data from the Biological and Economic Analysis Division (BEAD), empirical and default processing factors, and cooking factors derived from literature studies. Additionally, acute and steady-state TAFs of 3X and 8X, respectively, were applied for omethoate residues. EFED provided daily time-series outputs that simulate 29 years of residues in drinking water for 44 different application scenarios. These scenarios encompass both maximum (24 scenarios) and typical (20 scenarios) application rates for agricultural and non-agricultural uses of dimethoate. The drinking water distributions assume 100% conversion of dimethoate to omethoate[1] and incorporate the acute and steady-state TAF values. For steady-state assessments, 21-day rolling water averages were used to estimate 21-day average daily food and drinking water exposures.

The acute dietary (food only) exposure estimates exceed HED's level of concern (LOC; >100% of the acute population adjusted dose (aPAD)) for the U.S. population and all population subgroups at the 99.9th percentile. The U.S. population was 270% of the aPAD and children 1-2 years old, the most highly exposed population subgroup, was 640% of the aPAD. For the acute drinking water only runs, all (24) of the maximum application rate and 19 of the typical application rate drinking water scenarios resulted in risks of concern at the 99.9th percentile. Since the food alone and drinking water alone assessments result in risks of concern, acute food and drinking water analyses were not completed for all of the scenarios since they would also

[1] MRID 48041103 - Marin, J.E. 2010. Determination of the effect of chlorination on the degradation of dimethoate in water.

result in risks of concern at the 99.9th percentile. Overall, acute food and drinking water analyses were conducted for 27 (7 maximum application rate and 20 typical application rate) drinking water scenarios. All infants (<1 year old) was the most highly exposed population subgroup for 11 of the scenarios, with food and drinking water risk estimates that ranged from 710-1100% of the aPAD at the 99.9th percentile. Children 1-2 years old was the most highly exposed population subgroup for 16 of the scenarios, with food and drinking water risk estimates that ranged from 640-680% of the aPAD at the 99.9th percentile.

The food only steady-state results exceed HED's LOC (>100% of the steady-state population-adjusted dose (ssPAD)) for the U.S. population and all population subgroups at the 99.9th percentile. The U.S. population was 410% of the ssPAD and children 1-2 years old, the most highly exposed population subgroup, was 810% of the ssPAD. For the steady-state drinking water only analyses, all (24) of the maximum application rate and 19 of the typical application rate drinking water scenarios resulted in risks of concern at the 99.9th percentile. Since the food alone and drinking water alone assessments result in risks of concern, steady-state food and drinking water analyses were not completed for all of the scenarios since they would also result in risks of concern at the 99.9th percentile. Overall, food and drinking water steady-state analyses were conducted for 23 drinking water scenarios (3 maximum application rate and 20 typical application rate). All infants (<1 year old) was the most highly exposed population subgroup for six of the scenarios, with food and drinking water risk estimates that ranged from 970-1200% of the ssPAD at the 99.9th percentile. Children 1-2 years old was the most highly exposed population subgroups for 17 of the scenarios, with food and drinking water risk estimates that ranged from 810-880% of the ssPAD at the 99.9th percentile.

Residential (Non-Occupational) Exposure and Risk

All residential and other non-occupational uses of dimethoate were voluntarily cancelled, effective March 13, 2002 (Federal Register Notice/Vol. 67, No. 84/Wednesday, May 01, 2002/Notices/21669).

Non-Occupational Spray Drift Exposure and Risk

A quantitative non-occupational spray drift assessment was conducted for the registered uses of dimethoate. The assessment takes into consideration both dimethoate residues and residues of the major metabolite, omethoate. Adult dermal and children's (1 to < 2 year old) dermal and incidental oral risk estimates from indirect exposure related to spray drift exceed HED's level of concern (MOEs < 1000) at a range of distances from the edge of the field depending on the spray-drift scenario (e.g., 0 to >300 feet). Results indicate that the major spray-drift risk concerns are from aerial applications.

Volatilization/Residential Bystander

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The agency has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis, and during Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies) or further analyses are required for dimethoate.

Aggregate

The registered dimethoate uses are not anticipated to result in residential exposure and thus the acute and steady-state dietary exposure estimates represent the acute and steady-state aggregate exposure. Dimethoate is classified as a Group C carcinogen (possible human carcinogen). Quantification of risk using a non-linear approach will adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

Occupational Exposure and Risk

Occupational handler dermal and inhalation exposure and risk estimates were calculated for the registered uses of dimethoate. The occupational handler exposure and risk estimates indicate that the dermal and inhalation combined MOEs are of concern to HED (i.e., MOEs < 1000) for most scenarios assuming the use of label-required PPE. As was noted above, the inhalation risk estimates are considered to be a conservative estimate of exposure to dimethoate residues considering the inhalation POD was selected from an omethoate toxicity study. Only five scenarios (out of 40) reach an MOE above the LOC of 1000 at some level of PPE (above what is currently required on the labels) or with engineering controls.

Occupational post-application dermal exposure and risk estimates were assessed for all registered uses of dimethoate using submitted chemical-specific dislodgeable foliar residue (DFR) data. The post-application assessment takes into consideration both dimethoate residues and residues of the major metabolite, omethoate; both of which were measured in the available DFR studies. Based on the current exposure assessment, post-application risk estimates remain a concern in some situations for more than 30 days after application (i.e., MOEs < 1000). Current product-label REIs range from 48 hours to 24 days depending on the crop and geographic location (i.e., arid versus non-arid). Even though REIs of 12 and 24 hours may be long enough for MOEs to reach the LOC of 1000 for some crops/activities, HED recommends a minimum REI of 48 hours (72 hours in arid regions) to be protective of potential for exposure to omethoate which is known to form after application. These REIs are in line with the 40 CFR 156.208 (c) (2) assignments for active ingredients that are classified as Toxicity Category I for acute dermal, eye irritation, and primary skin irritation.

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for dimethoate at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for dimethoate.

Human Studies Review:

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from Pesticide Handler Exposure Database (PHED) 1.1, Outdoor Residential Exposure Task Force (ORETF), the Agricultural Handlers Exposure Task Force (AHETF) database, and the Agricultural Reentry Task Force (ARTF) database are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human

Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[2].

2.0 HED Recommendations

2.1 Data Deficiencies

There are no data deficiencies for the Registration Review eligibility of dimethoate.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

Plants: For the purpose of Registration Review, adequate methods are available for the enforcement of plant commodity tolerances. The Pesticide Analytical Manual (PAM) Vol. II lists three gas-liquid chromatography (GLC) methods (Methods A, B, and C) using flame photometric detection, and a colorimetric procedure (Method D) for analysis of residues of dimethoate and its oxygen analog in/on plant commodities. A second colorimetric procedure (Method E) is listed for the determination of residues of dimethoate *per se*. The limit of quantitation (LOQ) for the GLC methods is 0.05 ppm. A thin-layer chromatography (TLC) method is also listed (Method I) for determination of residues of dimethoate and its oxygen analog in/on plant commodities. The QuEChERS multiresidue method has also been validated for determination of dimethoate and omethoate (https://www.chromspec.com/pdf/e/uct19.pdf).

Livestock: For the purpose of Registration Review, an adequate method is available for the enforcement of livestock commodity tolerances. The method was modified from the QuEChERS multiresidue method. Briefly, samples are extracted with acetonitrile (ACN) or ACN/water (fat), shaken, and sonicated. The extract is partitioned with magnesium sulfate, sodium chloride, and a citrate buffer (sodium citrate dibasic sesquihydrate and sodium citrate tribasic dehydrate). The citrate buffer is not added for eggs. An aliquot of the organic layer extract is cleaned-up using dispersive solid-phase extraction (dSPE) PSA/ENVI-Carb SPE Clean-Up Tubes, filtered, diluted with ACN, and analyzed by liquid chromatography-mass spectroscopy/mass spectroscopy (LC-MS/MS) using electrospray ionization (ESI) in the positive-ion mode. The method monitors three ion transitions for determination of dimethoate and omethoate. The validated LOQ (determined as the lowest level of method validation, LLMV) is 0.001 ppm for each analyte in all livestock matrices. The reported limit of detection (LOD) is 0.0005 ppm for each analyte in egg, muscle, liver, kidney, and fat and 0.00025 ppm in milk.

Multiresidue Methods: The data requirements for multiresidue methods (MRMs) are fulfilled. The 1/94 Food and Drug Administration (FDA) PESTDATA database (PAM Volume I, Appendix I) indicates that residues of dimethoate and omethoate are completely recovered (>80%) by MRM Section 302 (Luke Method; Protocol D) but are not recovered by MRM Sections 303 (Mills, Onley, Gaither Method; Protocol E, nonfatty) and 304 (Mills fatty food method; Protocol E, fatty).

[2] http://www.epa.gov/pesticides/science/handler-exposure-data.html and http://www.epa.gov/pesticides/science/post-app-exposure-data.html

2.2.2 International Harmonization

U.S. permanent tolerances (listed in 40 CFR §180.204) plus Mexican, Canadian, and Codex maximum residue levels (MRLs) are summarized in Appendix G. The U.S. and Canadian residue definitions are harmonized (parent plus omethoate); however, the Codex residue definition is parent only. For some raw agricultural commodities, the levels of the tolerances/MRLs for the U.S., Canada, Mexico, and Codex are harmonized; however, there are many commodities for which the levels are not harmonized. Harmonization of the tolerance/MRL levels for beans, cauliflower, celery, pea, pepper, potato, tomato, turnip tops, and wheat, straw is not possible, as the U.S. use patterns require a higher tolerance. Harmonization of the tolerance/MRL levels for livestock meat byproducts, milk, egg, and citrus is not possible as the U.S. tolerances are significantly lower. Harmonization of the tolerance/MRL level for wheat, grain is possible as the U.S. tolerance level (0.04 ppm) is only slightly lower that the Codex MRL level (0.05 ppm).

2.2.3 Recommended Tolerances

Permanent tolerances have been established in 40 CFR §180.204 for the total residues of the insecticide dimethoate (*O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorodithioate) including its oxygen analog in/on various raw agricultural commodities ranging from 0.002 ppm to 5.0 ppm.

The tolerance expression for dimethoate [40 CFR §180.204(a)(1) and 40 CFR §180.204(c)] has been reviewed and should be updated as follows based on HED's Interim Guidance on Tolerance Expressions (S. Knizner, 27-MAY-2009).

> Tolerances are established for residues of the insecticide dimethoate, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of dimethoate (*O*,*O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorodithioate) and its oxygen analog (*O*,*O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorothioate), calculated as the stoichiometric equivalent of dimethoate, in or on the commodity.

A summary of the established and HED-recommended tolerances for residues of dimethoate can be found in Appendix D.

2.2.4 Revisions to Established Tolerances

HED is recommending for revisions to the tolerance expression in order to conform to current Agency policy. In addition, HED is recommending for the establishment of a tolerance for residues in/on fruit, citrus, group 10-10 concomitant with the deletion of the tolerances for residues in/on the individual members of the crop group; revocation of the tolerance for residues in/on sweet corn forage as there is no registered use on sweet corn; correction of the commodity definition for lima bean; increasing the tolerance for residues in/on ruminant meat byproducts and revocation of the tolerance for residues in/on poultry meat byproducts and eggs based on the results of new livestock feeding studies, and increasing the tolerance for residues in/on wheat grain in order to harmonize with the Codex MRL. HED previously recommended for establishment of tolerances for residues

in/on alfalfa seed and cotton gin byproducts and revisions to the tolerances for residues in/on livestock commodities (M. Sahafeyan; 24-MAY-2011; D232849) and for establishment of tolerances for residues in/on grass forage and hay (M. Sahafeyan; 12-NOV-2013; D239886). Additionally, the notation for blueberries in the e-40 CFR should be corrected to indicate that there are no U.S. registrations for blueberries as of August 16, 1996. Currently the e-CFR omits the word "no."

2.3 Label Recommendations

No label recommendations have been identified. A summary of the risk estimates has been provided, and shows that there are risk estimates of concern for registered uses of dimethoate based on the use information, label-required personal protective equipment (PPE; i.e., engineering controls), and REIs.

2.3.1 Recommendations from Residential Assessment

Adult dermal and children's (1 to < 2 year old) dermal and incidental oral risk estimates from indirect exposure related to spray drift exceed HED's LOC (MOEs < 1000) at a range of distances from the field depending on the spray-drift scenario (e.g., 0 to >300 feet) (see Section 6.4.1). Appropriate drift reduction technologies such as changing the spray type/nozzle configuration to coarser spray applications may result in less drift and reduced risk concerns (i.e., higher MOEs) from aerial applications. Similarly, using coarser sprays and lowering boom height for groundboom sprayers reduces risk concerns.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. Test Compound Nomenclature.

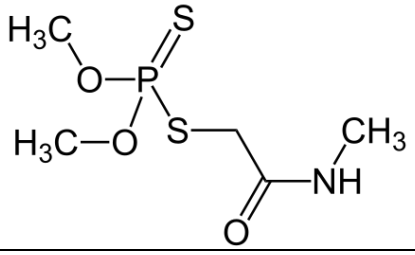
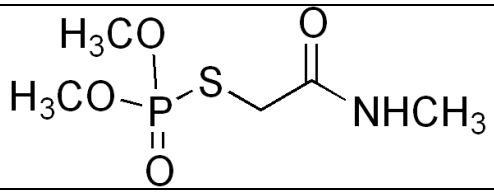
Chemical Structure	
Empirical Formula	$C_5H_{12}NO_3PS_2$
Common Name	Dimethoate
IUPAC name	*O,O*-dimethyl *S*-methylcarbamoylmethyl phosphorodithioate or 2-dimethoxyphosphinothioylthio-*N*-methylacetamide
CAS Name	*O,O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorodithioate
CAS Registry Number	60-51-5
End-use products	Dimate 4E, Dimethoate 4E, Cymate 267, Dimethoate 2.67 EC, etc.
Chemical Class	OP

Table 3.1. Test Compound Nomenclature.	
Chemical Structure	
Empirical Formula	$C_5H_{12}NO_4PS$
Common Name	Omethoate
IUPAC name	*O,O*-dimethyl *S*-methylcarbamoylmethyl phosphorothioate
CAS Name	*O,O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorothioate
CAS Registry Number	1113-02-6

3.2 Physical/Chemical Characteristics

Pure dimethoate is a colorless crystalline solid with an odor of mercaptan. Technical dimethoate (about 93% pure) varies from off-white crystals to a grey semi-crystalline material. Dimethoate is highly soluble in chloroform, methylene chloride, benzene, toluene, alcohols, esters, and ketones, slightly soluble in xylene, carbon tetrachloride, and aliphatic hydrocarbons, and partly soluble in water (log K_{OW} = 0.70) with a vapor pressure of 1.85 x 10^{-6} mm Hg at 20°C. A table of physical/chemical properties for dimethoate can be found in Appendix E.

3.3 Pesticide Use Pattern

There are numerous end-use product labels registered with dimethoate as the active ingredient including liquid and WSP formulations. The labeled use sites include various agricultural crops, Christmas tree farms, trees grown for pulp, and ornamentals in outdoor nurseries. Most of the registered products are applied via aerial, chemigation, airblast, groundboom, or with handheld equipment. For most use sites/crops, the maximum application rate is 2 lb ai/A, but for ornamentals in outdoor nurseries, the maximum application rate is 4.15 lb ai/A for airblast applications specifically. A summary of registered labels and dimethoate use directions are included in Appendix F.

3.4 Anticipated Exposure Pathways

Humans may be exposed to dimethoate, and its metabolite omethoate, in food and drinking water, since dimethoate may be applied directly to growing crops and application may result in dimethoate reaching sources of drinking water. There are no residential uses of dimethoate; however, there is the potential for short-term non-occupational exposure (dermal and incidental oral) to dimethoate and omethoate as a result of spray drift.

Based on the registered use pattern for dimethoate, short- and intermediate-term dermal and inhalation exposures are anticipated for occupational handlers and post-application workers. Occupational handlers are anticipated to be exposed to the parent, dimethoate, only. Occupational post-application workers may be exposed to residues of both dimethoate and omethoate

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://epa.gov/compliance/ej/resources/policy/exec_order_12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under the NHANES/WWEIA and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

Dimethoate is a member of the OP class of pesticides. Like other OPs, the initiating event in the AOP/MOA, for dimethoate involves inhibition of the enzyme AChE via phosphorylation of the serine residue at the active site of the enzyme. Dimethoate must be metabolized (activated) to the oxon metabolite (omethoate), which is the active AChE inhibiting moiety. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system (see Figure 1). For dimethoate and omethoate, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. AChE inhibition is the focus of this hazard characterization; the availability of reliable AChE inhibition dose response data is one of the key determinants in evaluating the toxicology database.

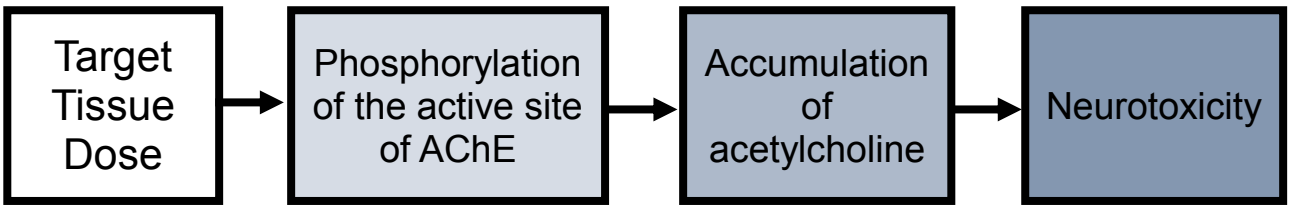


Figure 1. AOP for OPs.

4.1 Toxicology Studies Available for Analysis

The toxicology database for dimethoate is complete for risk assessment. The acceptable dimethoate studies available for risk assessment include:

- subchronic oral toxicity studies in rats and dogs

- chronic oral toxicity studies in rats and dogs
- carcinogenicity studies in rats and mice
- developmental studies in rats and rabbits
- reproduction toxicity study in rats
- acute and subchronic neurotoxicity studies in rats
- developmental neurotoxicity (DNT) study in rats
- acute and repeated comparative cholinesterase assays (CCA) in juvenile and adult rats
- special cross-fostering study in rats
- delayed neurotoxicity study in hens
- subchronic dermal toxicity study in rats
- *in vivo* dermal penetration studies in rats
- immunotoxicity study in mice
- mutagenicity studies
- metabolism studies in rats

Although never registered as an active ingredient in the U.S., omethoate has in the past been registered in other countries and, as a result, there is an extensive toxicity database for omethoate. The acceptable omethoate studies available for risk assessment include:

- chronic oral toxicity studies in rats and dogs
- carcinogenicity studies in rats and mice
- developmental studies in rats and rabbits
- reproduction toxicity studies in rats
- acute neurotoxicity study in rats
- acute and repeated CCA studies in rats
- special studies investigating AChE inhibition in rats and dogs
- delayed neurotoxicity study in hens
- repeated dosing inhalation study in rats
- mutagenicity studies
- metabolism studies in rats

Additionally studies have also been submitted demonstrating no significant AChE inhibition from multiple degradates of dimethoate, including hydroxy dimethoate, O-desmethyl omethoate carboxylic acid, des-o-methyl isodimethoate, O-desmethyl omethoate, and dimethoate carboxylic acid.

4.2 Absorption, Distribution, Metabolism, & Excretion (ADME)

4.2.1 Dimethoate

Dimethoate, like some other OPs, requires metabolic activation to its oxon metabolite (omethoate) to inhibit AChE, with subsequent metabolism that leads to detoxification. Generally, absorption and distribution are rapid with extensive metabolism and no accumulation in the tissues.

In a rat metabolism study, rats were administered [^{14}C]-dimethoate as a single oral dose (10 or 100 mg/kg), an intravenous dose (10 mg/kg), or 14-day repeated oral doses of dimethoate at 10 mg/kg followed by a single oral dose of [^{14}C]-dimethoate at 10 mg/kg. Dimethoate was rapidly absorbed, metabolized, and eliminated in rats for all dosing regimens. Consistent with the results of the AChE studies, there were no remarkable sex-, dose-, or treatment-related differences in the absorption, distribution, and elimination of dimethoate in rats. Dimethoate was absorbed and distributed quickly with time to peak plasma concentrations (T_{max}) reached less than 1 hour post-dosing. Total recovery of radioactivity ranged between 91% and 97% of the administered dose. Most of the radioactivity was excreted via the urine (85-91% of the dose). A small amount of radioactivity was found in feces (1-2% of the dose), in the tissues and remaining carcass (1-2% of the dose), and in the expired air as carbon dioxide (2-3% of the dose).

In the rat, dimethoate is metabolized via hydrolytic and oxidative pathways (based on urine analyses). The hydrolytic pathway (major) involves cleavage of the C-N bond to yield dimethoate carboxylic acid that was subsequently metabolized to dimethyldithiophosphate, dimethylthiophosphoric acid, and dimethylphosphoric acid. A minor metabolic pathway involves oxidation of dimethoate to its oxon analogue, omethoate, which was subsequently metabolized to dimethylthiophosphoric acid and dimethylphosphoric acid. Loss of the methoxy groups of the parent to yield carbon dioxide is a minor metabolic pathway.

4.2.2 Omethoate

In a rat metabolism study with omethoate, male and female rats exhibited signs of toxicity, including trembling, salivation, high breathing rate, and congestion of the eyes, at 0.5-4 hours post-dosing. Overall recovery of administered radioactivity was 88-98%. There were no remarkable sex-, dose-, or treatment-related differences in the absorption, distribution, and elimination of omethoate in rats. Absorption rates were rapid and T_{max} was reached within 1 hour post-dosing. Omethoate was excreted within 48 hours with the majority excreted via the urine (85-97% of the administered dose). The remainder of the administered radioactivity was excreted via the feces (2-4% of the administered dose). Biliary excretion was found to account for the majority of the fecal metabolite content. Based upon tissue burden data, omethoate and/or its metabolites do not appear to undergo any significant sequestration.

Omethoate appeared to be metabolized to a greater extent in males than in females as evidenced by higher percentages of parent compound remaining in urine from females and a higher percentage of omethoate metabolites in urine of males. The metabolite profile for urine included the parent compound (26-62% of the administered dose), *N*-methyl-2-(methylsulfinyl)-acetamide (16-35% of the administered dose), and *O*-desmethylated omethoate (4-9% of the administered dose). The same metabolites were also identified in the feces.

4.2.3 Dermal Absorption

There are two acceptable *in vivo* dermal penetration rat studies in the database for dimethoate. In the first study (MRID 43964001), dermal absorption (based on total amount of radioactivity recovered from urine, tissues, and feces after 6 hours of dermal exposure) was estimated to be 8-11% and 1-2% of the administered dose from rats treated at 10 and 100 mg/kg, respectively. There were no sex-related differences observed in absorption patterns. In the second study (MRID 45530501), dermal absorption (based on excreta, cage wash, and carcass) was estimated

at doses of 0.67 and 13.3 mg/kg to be approximately 6% after 1 hour of exposure and 25-38% after 10-24 hours of exposure. Since a route-specific dermal toxicity study was selected as the endpoint for dermal exposure assessments (see Section 4.5.1), a dermal absorption factor is not needed for this risk assessment.

4.3 Toxicological Effects

Dimethoate and omethoate have high-quality dose-response data across multiple lifestages, durations, and routes for both RBC and brain AChE inhibition. Many of these studies have been evaluated using BMD modeling techniques. BMD estimates are similar across age, sex, and method of administration (gavage, feeding, drinking water) for dimethoate and omethoate (Appendix 9 of USEPA 2004). High-quality studies in the dermal and inhalation routes with dimethoate and omethoate, respectively, allow for route-specific evaluation.

Using AChE inhibition as the critical endpoint for risk assessment purposes protects for other cholinergic effects, such as clinical signs, which are seen at doses much higher than those causing inhibition of AChE. In the case of dimethoate and omethoate, brain AChE inhibition provides the basis for human health risk extrapolations with the rat being the most sensitive species for dimethoate and omethoate exposures. Details of numerous dimethoate studies can be found in the toxicology disciplinary chapter for the Reregistration Eligibility Document (RED; P. Chin, 04-MAR-1997; D229308). Relevant omethoate studies are summarized in a 2005 review (P. Chin; 31-MAY-2005; TXR# 0051425).

In the acute and repeated CCA studies, juvenile rats, pregnant dams, fetuses and non-pregnant adults displayed similar results in both blood and brain measurements. In developmental and reproduction toxicity studies, AChE inhibition in fetuses/offspring was seen at or above dose levels eliciting inhibition in parental animals.

Increased qualitative susceptibility to offspring was observed in the toxicological databases. Several studies (i.e., range-finding and main DNT, cross-fostering, and one-generation reproductive toxicity studies with dimethoate, as well as the omethoate reproductive toxicity studies) demonstrate increased pup mortality following maternal exposure; however, the increased pup mortality occurred at doses at or above those causing decreased brain AChE activity in parental animals. The underlying basis of pup mortality is not fully understood though and the available data do not support maternal toxicity as being the only determinant of pup mortality. The pup mortality has been extensively reviewed by OPP and the Office of Research and Development (ORD) along with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP). A more detailed discussion of the pup mortality observations can be found in the revised post-SAP HED Chapter of the RED (D325201; 31-JAN-2006).

It has been concluded that regulation of dimethoate exposure at levels below those causing brain AChE inhibition will protect against brain AChE inhibition, as well as increased pup mortality, based on the following:

1) Comparison of benchmark dose levels for brain AChE inhibition and pup mortality following repeated dosing indicates that AChE inhibition occurs at doses similar to those associated with increases in pup mortality.

2) The evaluation of pup mortality data from the cross-fostering study reveals that increases in mortality from short-term exposures (10-15 doses) only occurred at the highest dose tested, indicating that increased mortality at lower doses requires longer durations of repeated dosing.
3) Comparison of the no-observed adverse-effect level (NOAEL) for increased pup mortality to the BMD_{10} for brain AChE inhibition following a single dose indicates that brain AChE inhibition occurs at doses below those causing a clear increase in pup mortality.

These conclusions regarding the interpretation of pup mortality seen in the dimethoate and omethoate database were supported by the 2005 FIFRA SAP. The SAP further supported the use of brain AChE inhibition for deriving PODs as protective of the pup mortality.

Dimethoate is classified as having low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Category III or IV). It was found to be a moderate eye irritant, but not a dermal irritant or dermal sensitizer. Omethoate is classified as acutely toxic via the oral, dermal, and inhalation routes (Toxicity Category I or II).

There was no evidence of immunotoxicity up to 36 mg/kg/day in a recently submitted immunotoxicity study with dimethoate (MRID 48572807 and 48997901).

Dimethoate is classified as a Group C carcinogen - possible human carcinogen (Memo; K. Dearfield; 29-AUG-1991). The classification is based upon equivocal hemolymphoreticular tumors in male B6C3F1 mice, the compound-related (no dose response) weak effect of combined spleen (hemangioma and hemangiosarcoma), skin (hemangiosarcoma), and lymph (angioma and angiosarcoma) tumors in male Wistar rats, and positive mutagenic activity associated with dimethoate. On June 25, 1992, the FIFRA SAP concurred with the Agency's classification of dimethoate as a Group C carcinogen. The Agency determined that quantification of risk using a non-linear approach would adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

4.3.1 Critical Durations of Exposure

One of the key elements in risk assessment is the appropriate integration of temporality between the exposure and hazard assessments. One advantage of an AOP understanding is that human health risk assessments can be refined, focused on the most relevant durations of exposure. The following text provides an analysis of the temporal pattern of AChE inhibition from acute (single) and repeated-dosing studies in laboratory animals for dimethoate. This analysis provides the basis for determining which exposure durations are appropriate for assessing human health risk. Table 4.3.1.1 provides a summary of the selected results from experimental toxicology studies with dimethoate.

Table 4.3.1.1. Dimethoate BMD_{10} and $BMDL_{10}$ Results (mg/kg/day) for Brain AChE Inhibition Over Time in Adult Rats.

Days of Dosing	Males		Females	
	BMD_{10}	$BMDL_{10}$	BMD_{10}	$BMDL_{10}$
1[a]	2.5	1.7	2.2	1.3
11[a]	0.49	0.37	0.37	0.27

14[a]	NA	NA	0.34	0.28
91[b]	0.40	0.29	0.48	0.40
205[c]	0.34	0.19	0.45	0.25

BMD_{10} = estimated dose where AChE is inhibited by 10% compared to background.
$BMDL_{10}$ = lower confidence bound on the BMD_{10}.
NA = not applicable; measurements at this time point were for pregnant females on gestational day 20.
[a] MRID 45529702 - CCA study.
[b] MRID 46348201 - One-generation range finding study.
[c] MRID 46181001 - Two-generation reproduction toxicity study.

As shown in Table 4.3.1.1, the acute (single-day) BMD values are the largest in the table, whereas BMD values from repeated exposures are remarkably similar. Although studies with AChE measurements were more limited with omethoate, a similar pattern was observed. OPs exhibit a phenomenon known as steady-state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady-state within 2-3 weeks, but this can vary among OPs. In the case of dimethoate, the results in Table 4.3.1.1 show a clear pattern of steady-state reached by 11 days of exposure. Given the results in Table 4.3.1.1 for dimethoate, acute (single-day) and steady-state durations are appropriate for human health risk assessment. As such, the endpoint selection discussed below focuses on acute (single-day) effects and steady-state effects.

Although there are data at a shorter time period than 21 days (i.e., 11 days), exposure assessments of 21 days and longer will be conducted for all routes of exposure (i.e., oral, dermal and inhalation) for all single chemical OP assessments. Although the durations of the toxicity and exposure assessments may differ, an exact match is not necessary and would suggest a level of precision that the toxicity data do not support. Given this, the 21-day and longer exposure assessment is scientifically supportable and also provides consistency with the OP cumulative risk assessment (OP CRA; 2002, 2006) and across the single chemical risk assessment for the OPs.

4.4 Literature Review on Neurodevelopment Effects

For the OPs, historically the Agency has used inhibition of AChE as the POD for human health risk assessment; at present time, this policy continues. This science policy is based on decades of work which shows that AChE inhibition is the initial event in the pathway to acute cholinergic neurotoxicity. The use of AChE inhibition data for deriving PODs was supported by the FIFRA SAP (2008, 2012) for chlorpyrifos as the most robust source of dose-response data for extrapolating risk and is the source of data for PODs for dimethoate/omethoate. A detailed review of the epidemiological studies used in this review can be found either in the 2014 chlorpyrifos revised draft human health risk assessment (D. Drew; 29-DEC-2014; D424485) or in the 2015 literature review for other organophosphates (OPP/USEPA; 15-SEP-2015; D331251).

Newer lines of research on OPs in the areas of potential AOPs, *in vivo* animal studies, and notably epidemiological studies in mothers and children, have raised some uncertainty about the agency's risk assessment approach with regard to the potential for neurodevelopmental effects in fetuses and children. Many of these studies have been the subject of review by the agency over the last several years as part of efforts to develop a risk assessment for chlorpyrifos (D. Drew;

29-DEC-2014; D424485). Initially, the agency focused on studies from three US cohorts: 1) The Mothers and Newborn Study of North Manhattan and South Bronx performed by the Columbia Children's Center for Environmental Health (CCCEH) at Columbia University; 2) the Mt. Sinai Inner-City Toxicants, Child Growth and Development Study or the "Mt. Sinai Child Growth and Development Study;" and 3) the Center for Health Assessment of Mothers and Children of Salinas Valley (CHAMACOS) conducted by researchers at University of California Berkeley. The agency has evaluated these studies and sought external peer review (FIFRA SAP reviews in 2008 and 2012; federal panel, 2013[3]) and concludes they are of high quality. In the three US epidemiology cohort studies, mother-infant pairs were recruited for the purpose of studying the potential health effects of environmental exposures during pregnancy on subsequent child development. Each of these cohorts evaluated the association between prenatal chlorpyrifos and/or OP exposure (with adverse neurodevelopmental outcomes in children through age 7 years). For the 2014 chlorpyrifos revised human health risk assessment (D. Drew; 29-DEC-2014; D424485), EPA included epidemiologic research results from these three US prospective birth cohort studies but primarily focused on the results of CCCEH since this cohort has published studies on the association between cord blood levels of chlorpyrifos and neurodevelopmental outcomes. The agency retained the FQPA 10X Safety Factor (SF) in the 2014 chlorpyrifos revised risk assessment, in large part, based on the findings of these studies.

In the 2015 updated literature review (OPP/USEPA; 15-SEP-2015; D331251), the agency conducted a systematic review expanding the scope of the 2012/2014 review focused on US cohort studies with particular emphasis on chlorpyrifos. The expanded 2015 review includes consideration of the epidemiological data on any OP pesticide, study designs beyond prospective cohort studies, and non-U.S. based studies. The updated literature review identified seven studies which were relevant (Bouchard et al., 2010; Fortenberry et al., 2014; Furlong et al., 2014; Guodong et al., 2012; Oulhote and Bouchard, 2013; Zhang et al., 2014; Shelton et al., 2014). These seven studies have been evaluated in context with studies from the 2012/2014 review (D. Drew; 29-DEC-2014; D424485). Only a brief summary is provided below.

The OP exposure being assessed in many of these studies used concentrations of urinary dialkyl phosphate metabolites (DAPs) as the urinary biomarker. Total DAPs is a non-specific measure of OP exposure and is the sum of six separate molecules - three dimethyl alkylphosphate (DMAP) molecules of DMP, DMTP, DMDTP, and three diethyl alkylphosphate (DEAP) molecules of DEP, DETP, and DEDTP. Each metabolite is a breakdown product from multiple OPs (Table 4.4.1; CDC, 2008)[4]. Specifically, DMP, DMTP, and DMDTP are associated with 18, 13, and 5 OPs, whereas DEP, DETP, and DEDTP are associated with 10, 10, and 4 OPs, respectively. Thus, using urinary DAPs alone as an exposure measure, it is not possible to separate the exposure and associated effects for single, specific OPs.

Table 4.4.1.CDC Table of organophosphate pesticides and their dialkyl phosphate metabolites (2008).

Pesticide	DMP	DMTP	DMDTP	DEP	DETP	DEDTP
Azinphos methyl	X	X	X			
Chlorethoxyphos				X	X	
Chlorpyrifos				X	X	
Chlorpyrifos methyl	X	X				

[3] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0170

[4] http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/l26opd_c_met_organophosphorus_pesticides.pdf

Coumaphos				X	X	
Dichlorvos (DDVP)	X					
Diazinon				X	X	
Dicrotophos	X					
Dimethoate	X	X	X			
Disulfoton				X	X	X
Ethion				X	X	X
Fenitrothion	X	X				
Fenthion	X	X				
Isazaphos-methyl	X	X				
Malathion	X	X	X			
Methidathion	X	X	X			
Methyl parathion	X	X				
Naled	X					
Oxydemeton-methyl	X	X				
Parathion				X	X	
Phorate				X	X	X
Phosmet	X	X	X			
Pirimiphos-methyl	X	X				
Sulfotepp				X	X	
Temephos	X	X				
Terbufos				X	X	X
Tetrachlorviphos	X					
Trichlorfon	X					

DMP = dimethylphosphate; DEP = diethylphosphate; DMTP = dimethylthiophosphate; DMDTP = dimethyldithiophosphate; DETP = diethylthiophosphate; DEDTP = diethyldithiophosphate.

For studies which measured urinary 3,5,6-trichloro-2-pyridinol (TCPy) (e.g., Fortenberry et al., 2014; Eskenazi et al., 2007; Whyatt et al., 2009), this metabolite can be derived from chlorpyrifos, chlorpyrifos-methyl, and the herbicide triclopyr. TCPy is also the primary environmental degradate of chlorpyrifos, chlorpyrifos-methyl, and triclopyr; thus exposure can be found directly on food treated with these pesticides. CCCEH studies have largely used chlorpyrifos measured in cord blood as the specific biomarker (e.g., Lovasi et al., 2010; Whyatt et al., 2004; Rauh et al., 2011). The CHARGE study (Shelton et al., 2015) did not measure biomarkers but instead used geospatial analysis to focus on the residential proximity to OP exposure using data from the California Department of Pesticide Regulation, with five OPs accounting for a total of 73% of the pesticide applied near residential settings (chlorpyrifos, acephate, diazinon, bensulide, and dimethoate).

Similarly, DAPs can be found directly on food following OP applications (Zhang et al, 2008; Chen et al, 2012). Specifically, studies have shown that DAPs may form as environmental degradates from abiotic hydrolysis, photolysis, and plant metabolism (Zhang et al, 2008; Chen et al, 2012; Racke et al, 1994). Furthermore, since these DAPs are excreted more rapidly and extensively than the parent OPs (Zhang et al, 2008; Forsberg et al, 2008), direct exposure to DAPs may lead to an overestimate of OP exposure when using urinary DAPs as a biomarker of OP exposure. The agency recognizes that this is a source of uncertainty when using DAPs for assessing OP exposure and will continue to monitor this issue in future assessments.

With respect to neurological effects near birth, the CHAMACOS and Mt. Sinai cohorts measured neurological effects at birth, and observed a putative association with total DEAP, total DMAP, and total DAP exposure (Engel et al., 2007; Young et al., 2005). Similarly, a Chinese study (Zhang et al., 2014) reported statistically significant associations between total DEAPs, total DMAPs, and total DAPs from prenatal OP pesticide exposure and neonatal neurodevelopment

assessed 3 days after birth. However, another cross-sectional Chinese study, Guodong et al (2012), observed no association with urinary DAPs and a developmental quotient score for 23-25 month old children.

The 3 US cohorts (CCCEH, Mt. Sinai, CHAMACOS) each reported evidence of impaired mental and psychomotor development, albeit not consistent by age at time of testing (ranging from 6 month to 36 months across the three cohorts). Attentional problems and ADHD were reported by three prospective cohorts [Rauh et al, 2006; Eskenazi et al., 2007; Marks et al, 2010; and Fortenberry et al (2014)] investigators with additional support from a case control study, Bouchard et al. (2010). The exposure metric varied among these studies. Specifically, Fortenberry et al (2014) found suggestive evidence of an association with TCPy and ADHD in boys whereas statistically significant associations were observed by Rauh et al (2006) with chlorpyrifos exposure and ADHD. Eskenazi et al (2007) reported associations with total DMAPs and total DAPs and ADHD; Marks et al (2010) reported associations with total DEAP, DMAP, and total DAP exposure and ADHD. In a national cross-sectional study of Canadian children, using 2007-2009 data for children age 6-11 years (Oulhote and Bouchard, 2013), there were no overall statistically significant associations observed between child urinary DEAP, DMAP, or total DAP metabolite levels and parentally reported behavioral problems. In contrast, Bouchard et al. (2010), looking at U.S. children age 8-15 years in the 2000-2004 National Health and Nutrition Examination Survey (NHANES), observed a positive association between attention and behavior problems and total DAPs and DMAPs, but not DEAPs. As part of their analysis, Oulhote and Bouchard (2013) noted that their outcome assessment for behavioral problems may not have been as sensitive as Bouchard et al (2010), which may in part account for the difference in the observed results from these studies.

In addition, the three US cohorts and the CHARGE study have reported suggestive or positive associations between OP exposure and autism spectrum disorders (Rauh et al., 2006; Shelton et al., 2014; Eskenazi et al, 2007; Furlong et al., 2014). Specifically, Furlong et al (2014) documented suggestive evidence of an association between total DEAP exposure and reciprocal social responsiveness among blacks and boys. Eskenazi et al (2007) reported a statistically significant association between pervasive developmental disorder (PDD) and total DAP exposure, whereas Eskenazi et al (2010) reported non-significant, but suggestive, increased odds of PDD of 2.0 (0.8 to 5.1; p=0.14). Rauh et al (2006) documented a significant association between PDD and specifically chlorpyrifos exposure. Both PDD and reciprocal social responsiveness are related to the autism spectrum disorder. Using a different exposure assessment method (geospatial analysis and residential proximity to total OP exposure), Shelton et al (2014) also showed statistically significant associations between total OP exposure and ASD. While these studies vary in the magnitude of the overall strength of association, they have consistently observed a positive association between OP exposure and ASD. Finally, CCCEH, Mt. Sinai, CHAMACOS have reported an inverse relation between the respective prenatal measures of chlorpyrifos and intelligence measures at age 7 years (Rauh et al. ,2011; Engel et al., 2011; Bouchard et al., 2011).

Across the epidemiology database of studies, the maternal urine, cord blood, and other (meconium) measures provide evidence that exposure did occur to the fetus during gestation but the actual level of such exposure during the critical window(s) of susceptibility is not known. While significant uncertainties remain about the actual exposure levels experienced by mothers and infant participants in the children's health cohorts, it is unlikely that these exposures resulted

in AChE inhibition. As part of the CHAMACOS study, Eskenazi et al. (2004) measured AChE activity and showed that no differences in AChE activity were observed. The biomarker data (chlorpyrifos) from the Columbia University studies are supported by the agency's dose reconstruction analysis using the PBPK-PD model (D424485, D. Drew et al, 12/29/2014). Following the recommendation of the FIFRA SAP (2012), the agency conducted a dose reconstruction analysis of residential uses available prior to 2000 for pregnant women and young children inside the home. The PBPK-PD model results indicate for the highest exposure considered (i.e., indoor broadcast use of a 1% chlorpyrifos formulation) <1% RBC AChE inhibition was produced in pregnant women. While uncertainty exists as to actual OP exposure at (unknown) critical windows of exposure, EPA believes it is unlikely individuals in the epidemiology studies experienced RBC AChE inhibition.

A review of the scientific literature on potential modes of action/adverse outcome pathways (MOA/AOP)[5] leading to effects on the developing brain was conducted for the 2012 FIFRA SAP meeting (USEPA, 2012) and updated for the December 2014 chlorpyrifos revised risk assessment (D. Drew; 29-DEC-2014; D424485). In short, multiple biologically plausible hypotheses and pathways are being pursued by researchers that include targets other than AChE inhibition, including cholinergic and non-cholinergic systems, signaling pathways, proteins, and others. However, no one pathway has sufficient data to be considered more credible than the others. The fact that there are, however, sparse AOP data to support the *in vitro* to *in vivo* extrapolation, or the extrapolation from biological perturbation to adverse consequence significantly limits their quantitative use in risk assessment. The SAP concurred with the agency in 2008 and 2012 about the lack of definable key events in a MOA/AOP leading to developmental neurobehavioral effects. However, since the 2014 literature review, there are no substantive changes in the ability to define and quantitate steps in an MOA/AOP leading from exposure to effects on the developing brain. Published and submitted guideline DNT laboratory animal studies have been reviewed for OPs as part of the 2012/2014 review (D424485, D. Drew et al, 12/29/2014) and the updated 2015 review (OPP/USEPA; 15-SEP-2015; D331251). Neurobehavioral alterations in laboratory animals were often reported, albeit at AChE inhibiting doses, but there was generally a lack of consistency in terms of pattern, timing, or dose-response for these effects, and a number of studies were of lower quality. However, this information does provide evidence of long-lasting neurodevelopmental disorders in rats and mice following gestational exposure.

At this time, a MOA(s)/AOP(s) has/have not been established for neurodevelopmental outcomes. This growing body of literature does demonstrate, however, that OPs are biologically active on a number of processes that affect the developing brain. Moreover, there is a large body of *in vivo* laboratory studies which show long-term behavioral effects from early life exposure, albeit at doses which cause AChE inhibition. EPA considers the results of the toxicological studies relevant to the human population, as qualitatively supported by the results of epidemiology studies. The agency acknowledges the lack of established MOA/AOP pathway and uncertainties associated lack of ability to make strong causal linkages and unknown window(s) of susceptibility. These uncertainties do not undermine or reduce the confidence in the findings of the epidemiology studies. The epidemiology studies reviewed in the 2012/2014 and 2015 literature reviews represent different investigators, locations, points in time, exposure assessment procedures, and outcome measurements. Despite all these differences in study design, with the

[5] Mode of action (MOA) and adverse outcome pathways (AOPs) describe a set of measureable key events that make up the biological processes leading to an adverse outcome and the causal linkages between such events.

exception of two negative studies in the 2015 literature review (Guodong et al, 2012; Oulhote and Bouchard, 2013), authors have identified associations with neurodevelopmental outcomes associated with OP exposure across four cohorts and twelve study citations. Specifically, there is evidence of delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children who were exposed to OPs during gestation. Investigators reported strong measures of statistical association across several of these evaluations (odds ratios 2-4 fold increased in some instances), and observed evidence of exposures-response trends in some instances, *e.g.*, intelligence measures.

As section 408(b)(2)(C) of the FFDCA instructs EPA, in making its "reasonable certainty of no harm" finding, that in "the case of threshold effects, an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children." Section 408 (b)(2)(C) further states that "the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children." Given the totality of the evidence, there is sufficient uncertainty in the human dose-response relationship for neurodevelopmental effects which prevents the agency from reducing or removing the statutory 10X FQPA Safety Factor. For the dimethoate DRA, a value of 10X has been applied. Similarly, a database uncertainty factor of 10X will be retained for occupational risk assessments. The agency will continue to evaluate the epidemiology studies and pursue approaches for quantitative or semi-quantitative comparisons between doses which elicit AChE inhibition and those which are associated with neurodevelopmental outcomes prior to a revised human health risk assessment.

4.5 Safety Factor for Infants and Children (FQPA SF)

As noted above, the lack of an established MOA/AOP makes quantitative use of the epidemiology studies in risk assessment challenging, particularly with respect to determining dose-response, critical duration of exposure, and window(s) of susceptibility. However, exposure levels in the range measured in the epidemiology studies are likely low enough that they are unlikely to result in AChE inhibition. Epidemiology studies consistently identified associations with neurodevelopmental outcomes associated with OP exposure such as delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children. Therefore, there is a need to protect children from exposures that may cause these effects; this need prevents the agency from reducing or removing the statutory FQPA Safety Factor. **Thus, the FQPA 10X Safety Factor will be retained for dimethoate/omethoate for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.**

4.5.1 Completeness of the Toxicology Database

The existing toxicological databases are complete and adequate for characterizing dimethoate and omethoate toxicity. Available dimethoate studies for FQPA evaluation include developmental studies in the rat and rabbit, reproductive toxicity studies, CCA studies, neurotoxicity studies (acute, subchronic, and developmental), and a special cross-fostering study.

Available omethoate studies for FQPA evaluation include CCA studies, developmental studies in the rat and rabbit, reproductive toxicity studies, and an acute delayed hen neurotoxicity study.

As discussed in Section 4.4, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.2 Evidence of Neurotoxicity

Dimethoate and omethoate are OPs with an established neurotoxic AOP. AChE inhibition is the most sensitive effect in all species, routes, and lifestages and is being used in deriving the PODs.

4.5.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

There is no evidence of increased quantitatively sensitivity/susceptibility to offspring following exposure to dimethoate/omethoate based on AChE inhibition. In some studies, increased pup mortality was observed at doses causing decreased brain AChE activity in parental animals indicating increased qualitative susceptibility. Regulation of dimethoate exposure at levels below those causing brain AChE inhibition will protect against brain AChE inhibition in adults and offspring, as well as the observed increase in pup mortality (see Section 4.3).

As discussed in Section 4.4, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.4 Residual Uncertainty in the Exposure Database

There are no residual uncertainties with regard to dietary and occupational exposure assessments. The dietary exposure assessments use PDP data, PCT estimates, empirical and default processing factors, cooking factors derived from literature studies, and the acute and steady-state TAFs which account for the greater toxicity of the omethoate metabolite. The food and water dietary assessments incorporate 29 years of modeled water residues which assume 100% conversion of dimethoate to omethoate and were adjusted using the acute and steady-state TAFs. Although data were used to refine the dietary exposure assessments, the assessments are not expected to underestimate dietary (food and water) exposures.

4.5 Toxicity Endpoint and Point of Departure Selections

4.5.1 Dose-Response Assessment

Table 4.5.4.1 summarizes the dimethoate toxicity endpoints and PODs selected from an evaluation of the database. This endpoint selection was based on a weight of the evidence evaluation using the following considerations:

- *Relative sensitivity of the brain and RBC compartments*: For dimethoate and omethoate, across most studies, durations, lifestages, and routes, the brain is similarly or more

sensitive than RBCs. As such, OPP has emphasized the brain data in POD derivation as these data represent the target tissue and brain data tend to be less variable than RBC data.

- *Potentially susceptible populations (fetuses, juveniles, pregnancy*): The available AChE data across multiple lifestages (adults, pregnant adults, fetuses, juveniles) show no quantitative lifestage sensitivity for dimethoate and omethoate. In several studies, increased pup mortality was observed at doses at or above those causing decreased brain AChE activity in parental animals.
- *Route of exposure:* It is preferred to match, to the degree possible, the route of exposure in the toxicity study with that of the exposure scenario(s) of interest. There are oral and dermal studies with dimethoate, as well as an inhalation study with omethoate, which contain high-quality dose-response AChE data.
- *Duration of exposure:* It is preferred to match, to the degree possible, the duration of toxicity study with that of the exposure duration of interest. There are single-day and steady-state oral studies, but only steady-state dermal and inhalation studies are available.
- *Consistency across studies:* In cases where multiple datasets are available for a single duration, it is important to evaluate the extent to which data are consistent (or not) across studies. The dimethoate and omethoate databases have striking consistency across studies, which allows the PODs to be derived from multiple critical studies, thereby increasing the confidence in such values.

Consistent with risk assessments for other AChE-inhibiting compounds, OPP has used a benchmark response (BMR) level of 10% and has thus calculated BMD_{10} and $BMDL_{10}$ values (See Appendix B for summary of OPP's ChE policy). The BMD_{10} is the estimated dose where AChE is inhibited by 10% compared to background. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}. As a matter of science policy, the Agency uses the BMDL, not the BMD, for use as the POD (USEPA, 2012). All BMD/BMDL modeling for all individual datasets was completed using USEPA BMD Software to fit an exponential model to the data. BMD results from the OP CRA (2002, 2006) were included in the endpoint selection weight-of-evidence evaluation.

Studies used for endpoint selection are supported by the 2005 FIFRA SAP. BMD values for studies applicable to endpoints selection (dimethoate CCA, dimethoate dermal, and omethoate inhalation studies) were recalculated using up-to-date BMD software, which resulted in slight adjustments in the POD values derived from the acute dimethoate CCA study (MRID 45529702) and the dimethoate dermal toxicity study (MRID 44999101). The TAFs for omethoate were derived using BMD_{10} values (see Section 4.5.2). All remaining POD values did not change from the RED. This approach is consistent with the OP CRA and the previous dimethoate RED document (C. Jarvis; 31-JAN-2006; D325201).

Summary tables of BMD analyses can be found in Appendix C and the technical details of the analysis can be found in the BMD analysis memo (M. Perron; 15-SEP-2015; TXR# 0057249).

Acute Dietary (all populations)

A POD for the acute dietary (all populations) exposure scenario was derived from the results of a high-quality, well-conducted dimethoate CCA rat study (MRID 45529702). A $BMDL_{10}$ of 0.91 mg/kg/day associated with brain AChE inhibition in PND11 female pups was selected as a

suitable POD for the acute dietary (all populations) exposure scenario. The corresponding BMD_{10} was 1.55 mg/kg/day.

Brain AChE inhibition was selected for the POD since the brain is a principal target organ for OP pesticides and the brain AChE data was more robust than RBC AChE data. Data from the PND11 pups represent highly exposed sub-populations (infants and young children) and thus are appropriate for POD derivation.

An uncertainty factor of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)) is applied to the $BMDL_{10}$ to obtain an aPAD of 0.00091 mg/kg/day for exposure scenarios with infants, children, youths, and women of childbearing age. The only population subgroup that the FQPA SF is not retained for is adults 50-99; therefore, the aPAD for this population subgroup is 0.0091 mg/kg/day.

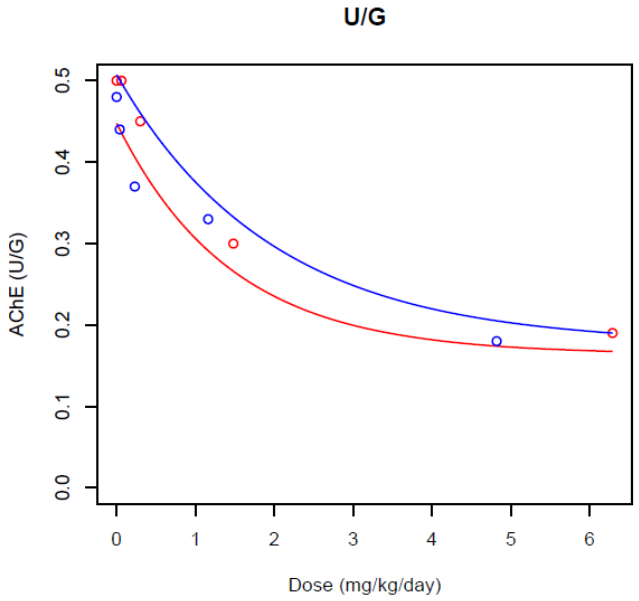
Steady-State Dietary (all populations)

There is remarkable similarity in BMD estimates across multiple dimethoate studies, durations, lifestages, and compartments in studies 11 days and longer (Table 4.3.1.1; Appendix 9 of USEPA 2004). Because of this consistency, OPP has elected to use BMD/BMDL estimates reported in the OP CRA (2002, 2006) for deriving the steady-state oral POD. Results of the OP CRA incorporate multiple time points together in a single BMD/BMDL analysis and are thus highly robust. Specifically, in the OP CRA, EPA performed a sophisticated statistical analysis using nonlinear mixed effects models that allow for combining the results of multiple studies and multiple time points into a single BMD estimate. These procedures were reviewed favorably by the FIFRA SAP in February 2002.

For the OP CRA, the available AChE data for dimethoate at durations of 21 days and longer in adult rats were extracted from the combined chronic oral toxicity/carcinogenicity study in rats (MRID 00164177). The plot of the brain AChE data from this study can be found in Figure 4.5.1.1. A $BMDL_{10}$ of 0.22 mg/kg/day associated with brain AChE inhibition in male and female adult rats was selected as a suitable POD for the steady-state dietary (all populations) exposure scenario. The corresponding BMD_{10} was 0.25 mg/kg/day.

An uncertainty factor of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)) is applied to the $BMDL_{10}$ to obtain a ssPAD of 0.00022 mg/kg/day for exposure scenarios with infants, children, youths, and women of childbearing age. The only population subgroup that the FQPA SF is not retained for is adults 50-99; therefore, the ssPAD for this population subgroup is 0.0022 mg/kg/day.

Figure 4.5.1.1. BMD Results (Red = males; Blue = females) from the OP CRA (2002, 2006) for Dimethoate (extracted from USEPA, 2002, Appendix III.B).



Incidental Oral, Steady-State

For the purpose of assessing potential risk associated with incidental oral exposure from steady-state durations, OPP selected the dose and endpoint from the OP CRA, which is based on available AChE data for dimethoate at durations of 21 days and longer in adult rats from the combined chronic oral toxicity/carcinogenicity study in rats (USEPA, 2002 and 2006). Quantitation of incidental oral risks was performed using the $BMDL_{10}$ value of 0.22 mg/kg and the BMD_{10} of 0.25 mg/kg based on brain AChE inhibition. These values do not specifically represent the subpopulations of interest (infants, toddlers, young children) for incidental oral exposure; however, there was no evidence of quantitative susceptibility in repeated dosing studies. A total uncertainty factor of 1000X is appropriate for incidental oral exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and 10X FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

Dermal, Steady-State

A dermal POD was selected from a 28-day dermal dimethoate toxicity study (MRID 44999101) in rats based on brain AChE inhibition in female rats ($BMDL_{10}$ = 20.2 mg/kg/day; BMD_{10} = 28.5 mg/kg/day). A total uncertainty factor of 1000X is appropriate for dermal exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF for residential assessments or as a database uncertainty factor in occupational assessments due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

Inhalation Steady-State

A route-specific inhalation toxicity study with dimethoate is not available to assess AChE inhibition due to repeated exposure. An inhalation POD was selected from a 28-day inhalation toxicity study with omethoate (MRID 46358601) based on brain AChE inhibition in male rats ($BMDL_{10}$ = 0.38 mg/m^3/day or 0.00038 mg/L/day; BMD_{10} = 0.51 mg/m^3/day or 0.00051

mg/L/day). Due to the lack of characterization of particle sizes in the study, the mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) could not be determined. As a result, human-equivalent concentrations could not be estimated for the systemic effects (AChE inhibition) from inhalation exposure. For occupational scenarios, duration adjustments were made to extrapolate exposure in the animal study (6 hours/day; 5 days/week) to a typical occupational exposure (8 hours/day; 5 days/week). The resulting duration adjusted value for occupational exposures is 0.285 mg/m^3. For estimating occupational inhalation risks from different occupational activities, inhalation doses of 0.016, 0.033, and 0.057 mg/kg/day corresponding to the breathing rates of 8.3, 16.7, or 29 L/min were calculated using this duration adjusted value. For inhalation exposures, a total uncertainty factor of 1000X was applied (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X database uncertainty factor in occupational assessments due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)).

4.5.2 Toxicity Adjustment Factors for Omethoate

As the oxon metabolite of dimethoate, omethoate has been found to be a more potent AChE inhibitor. To account for the increased potency of omethoate in risk estimates, BMD modeling was used to evaluate relative potency for dimethoate and omethoate and to estimate the TAFs for acute and steady-state exposure durations. As described in the guidance document for CRA (USEPA, 2002), comparisons of toxic potency should be made using a uniform basis of comparison, by using to the extent possible a common response derived from a comparable measurement methodology, species, and sex for all the exposure routes of interest. Dose-response modeling is preferred over the use of no- or lowest-observed adverse-effect levels (NOAELs/LOAELs) for determining relative toxic potency. NOAELs and LOAELs do not necessarily reflect the relationship between dose and response for a given chemical, nor do they reflect a uniform response across different chemicals.

TAFs have been estimated previously for dimethoate and omethoate (A. Lowit; 11-APR-2005; TXR# 0052940). Updated acute TAFs were calculated since previous values were based only on the limited data available at that time. Recently received omethoate CCA data can be incorporated into the acute analysis to derive sex- and age-specific values. To calculate acute TAFs, BMD_{10} values obtained from the acute CCAs in adult and juvenile rats were utilized. The sex- and age-specific acute TAF applied to residues of omethoate corresponds to the age and sex of the animal used for endpoint selection (i.e., the acute TAF of 8 will be used to assess acute dietary exposures because the POD value is based on brain AChE inhibition in female PND11 pups).

The originally calculated steady-state TAF of 3 was derived using the BMD_{10} values from the combined chronic oral toxicity/carcinogenicity study for dimethoate and a 28-day subchronic oral toxicity study for omethoate (A. Lowit; 24-APR-2002; TXR# 0050651). This value has since been verified using data from a two-year feeding study with omethoate; therefore, no changes were made to the steady-state TAF (A. Lowit; 10-JUL-2002; TXR# 0050901).

Table 4.5.2.1. Acute TAFs[a] Calculated for Adult and Juvenile Rats Using BMD of Brain AChE Inhibition After a Single Dose.

	Male	Female

Adults		
Dimethoate BMD_{10} (mg/kg/day)	2.5	2.2
Omethoate BMD_{10} (mg/kg/day)	0.2	0.3
Acute TAF	13	7
Pups (PND11)		
Dimethoate BMD_{10} (mg/kg/day)	1.8	1.6
Omethoate BMD_{10} (mg/kg/day)	0.2	0.2
Acute TAF	9	8

[a] TAF = dimethoate BMD_{10} ÷ omethoate BMD_{10}.

4.5.3 Recommendation for Combining Routes of Exposures for Risk Assessment

When there are potential occupational and residential exposures to a pesticide, the risk assessment must address exposures from three major sources (oral, dermal, and inhalation) and determine whether the individual exposures can be combined if they have the same toxicological effects. PODs for the incidental oral, dermal, and inhalation routes are all derived from brain AChE inhibition. As a result, exposure from all routes can be combined.

4.5.4 Cancer Classification and Risk Assessment Recommendation

Dimethoate is classified as a Group C carcinogen - possible human carcinogen (Memo; K. Dearfield; 29-AUG-1991). On June 25, 1992, the FIFRA SAP concurred with the Agency's classification of dimethoate as a Group C carcinogen. Quantification of risk using a non-linear approach will adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

4.5.5 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Table 4.5.5.1. Summary of Toxicological Doses and Endpoints for Dimethoate for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	POD	UFs[a]	LOC	Study and Toxicological Effects
Acute Dietary (all populations except adults 50-99 years old)	$BMDL_{10}$ = 0.91 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X	aRfD = 0.00091 aPAD = 0.00091	CCA study in rats (MRID 45529702) BMD_{10} = 1.55 mg/kg/day Inhibition of brain AChE in female rat pups.
Acute Dietary (adults 50-99 years old)	$BMDL_{10}$ = 0.91 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	aRfD = 0.0091 aPAD = 0.0091	CCA study in rats (MRID 45529702) BMD_{10} = 1.55 mg/kg/day Inhibition of brain AChE in female rat pups.
Steady-State Dietary (all populations except adults 50-99 years old)	$BMDL_{10}$ = 0.22 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X	ssRfD = 0.00022 ssPAD = 0.00022	Combined chronic oral toxicity/carcinogenicity study (OP CRA 2002, 2006; MRID 00164177) BMD_{10} = 0.25 mg/kg/day Inhibition of brain AChE in adult rats.

Table 4.5.5.1. Summary of Toxicological Doses and Endpoints for Dimethoate for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	POD	UFs[a]	LOC	Study and Toxicological Effects
Steady-State Dietary (adults 50-99 years old)	$BMDL_{10}$ = 0.22 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	ssRfD = 0.0022 ssPAD = 0.0022	Combined chronic oral toxicity/carcinogenicity study (OP CRA 2002, 2006; MRID 00164177) BMD_{10} = 0.25 mg/kg/day Inhibition of brain AChE in adult rats.
Incidental Oral Steady-State	$BMDL_{10}$ = 0.22 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X	Residential LOC for MOE < 1000	Combined chronic oral toxicity/carcinogenicity study (OP CRA 2002, 2006; MRID 00164177) BMD_{10} = 0.25 mg/kg/day Inhibition of brain AChE in adult rats.
Dermal Steady-State	$BMDL_{10}$ = 20.2 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X	Residential LOC for MOE < 1000	28-day rat dermal toxicity (MRID 44999101) BMD_{10} = 28.5 mg/kg/day Inhibition of brain AChE in adult rats.
Cancer (oral, dermal, inhalation)	Classification: Group C carcinogen (possible human carcinogen).			

Point of departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, ss = steady-state). RfD = reference dose (a = acute, ss = steady-state). MOE = margin of exposure. LOC = level of concern. BMD_{10} = estimated dose where AChE is inhibited by 10% compared to background. $BMDL_{10}$ = lower confidence bound on the BMD_{10}.

[a] FQPA SF retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). This includes all exposure scenarios, except the dietary exposure scenarios for the population subgroup adults 50-99 for which the FQPA SF has been reduced to 1X.

Table 4.5.5.2. Summary of Toxicological Doses and Endpoints for Dimethoate for Use in Occupational Human Health Risk Assessments.

Exposure/ Scenario	POD	UFs	LOC	Study and Toxicological Effects
Dermal Steady-State	$BMDL_{10}$ = 20.2 mg/kg/day	UF_A = 10X UF_H = 10X UF_{DB} = 10X[b]	Occupational LOC for MOE < 1000	28-day rat dermal toxicity (MRID 44999101) BMD_{10} = 28.5 mg/kg/day Inhibition of brain AChE in adult rats.
Inhalation Steady-State	$BMDL_{10}$ = 0.38 mg/m^3/day[a]	UF_A = 10X UF_H = 10X UF_{DB} = 10X[b]	Occupational LOC for MOE < 1000	Omethoate 21-day inhalation rat study (MRID 46358601) BMD_{10} = 0.51 mg/m^3/day Inhibition of brain AChE in adult rats.
Cancer (oral, dermal, inhalation)	Classification: Group C carcinogen (possible human carcinogen).			

Point of departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC

= level of concern. BMD_{10} = estimated dose where AChE is inhibited by 10% compared to background. $BMDL_{10}$ = lower confidence bound on the BMD_{10}.
[a] Inhalation doses corresponding to the breathing rates of 8.3, 16.7, and 29 L/min were calculated as 0.016, 0.033, and 0.057 mg/kg/day, respectively, for occupational activities using a duration adjusted value of 0.285 mg/m^3.
[b] UF_{DB} for occupational dermal and inhalation exposures = database uncertainty factor due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4)

4.6 Endocrine Disruption

As required by FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic, and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints that may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for dimethoate, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), dimethoate is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[6] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

Dimethoate is on List 1 for which EPA has received all the required Tier 1 assay data. The Agency has reviewed all of the assay data received for the appropriate List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets (see EPA-HQ-OPP-2009-0059). For further information on the status of the EDSP, the policies and

[6] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[7]

5.0 Dietary Exposure and Risk Assessment

5.1 Metabolite/Degradate Residue Profile

5.1.1 Summary of Plant and Animal Metabolism Studies

The qualitative nature of the residue in plants is adequately understood. Dimethoate is readily taken up and translocated by plants, and is metabolized hydrolytic and oxidative processes to omethoate, dimethoate carboxylic acid, dimethyl hydrogen phosphate and *O,O*-dimethyl hydrogen phosphorodithioate, indicating oxidation to omethoate, omethoate carboxylic acid, and dimethoate carboxylic acid, and cleavage of the P-S linkage either before or after oxidation. The residues to be regulated in plants are dimethoate and its oxygen analog, omethoate. The current tolerance expression for plant commodities is adequate.

In the confined rotational crop study, a substantial proportion of the residue was characterized as polar compounds or polar hydroxy compounds. Based on the current studies and registered rates, inadvertent residues dimethoate and omethoate in rotational crops are expected to be insignificant; the low residue levels consisted mainly of polar metabolites.

The qualitative nature of the residue in eggs, poultry tissues, and ruminant tissue is adequately understood. The available livestock metabolism data indicate that metabolism occurs via conversion of dimethoate to omethoate, followed by cleavage of the P-S bond resulting in phosphorylation of natural products. The established tolerances for dimethoate residues in livestock commodities are currently expressed in terms of the total residues of dimethoate and its oxygen analog, omethoate.

5.1.2 Summary of Environmental Degradation

Dimethoate is highly mobile and relatively non-persistent. The primary route of dissipation is microbially mediated hydrolytic and oxidative degradation in aerobic soil, particularly under moist conditions, with a half-life of 2.2 days. Dimethoate does not photodegrade. Volatilization of dimethoate from the soil surface appears to be moderate and it is not expected to be a significant route of dissipation compared to other routes of dissipation. It hydrolyzes very slowly in sterile buffered solutions at pHs 5 and 7 (156 and 68 days, respectively), but hydrolyzes rapidly to desmethyl dimethoate and dimethyl thiophosphoric acid with a half-life of 4.4 days at pH 9. The anaerobic half-life was found to be approximately 22 days, with the major non-volatile degradate being desmethyl dimethoate. Once dimethoate is applied by foliar application, it is expected to reach the crop, but it can also be transported offsite by spray drift and/or surface (dissolved) runoff occurring within days to weeks after applications. The chemical is not expected to leach substantially due to its relatively low persistence in soil. Dimethoate is systemic (although it also has contact activity), so it is also expected to move through vegetation and/or root systems. The primary toxic degradate, omethoate, was found under field conditions in the top layer (0-6") of soil in all five field studies, though it was not

[7] http://www.epa.gov/endo/

detected in the laboratory degradation and/or soil and sediment metabolism studies. The presence of omethoate has been established through field studies in insects, plants, and mammals. It is also formed during drinking water treatment. Omethoate was the only degradate analyzed in the dimethoate field-dissipation study. The other degradates identified in the laboratory studies were not included in the analysis because it is believed that: 1) based on the aerobic soil metabolism study, they would not persist in the field; and, 2) they are not toxicologically significant.

5.1.3 Comparison of Metabolic Pathways

Extensive studies have been conducted on the metabolism of dimethoate in both plants and mammals. The major route of metabolism in mammals appears to be through the thiocarboxy derivative to the corresponding dimethyl esters of phosphoric, thiophosphoric, or dithiophosphoric acids. The oxygen analog of dimethoate forms in animals, although this route is minor with respect to the principle route. In plants, the formation of the oxygen analog is a major route of metabolism. However, various investigators are not in agreement regarding the quantitative nature of this oxidation route, nor are they in agreement on quantitative nature of the other pathways of metabolism, which involve hydrolysis and demethylation.

5.1.4 Residues of Concern Summary and Rationale

The residue of concern in crops and livestock, for purposes of tolerance enforcement and risk assessment are dimethoate (dimethoate (*O*,*O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorodithioate) and omethoate, its oxygen analog, (*O*,*O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorothioate. The residues of concern in drinking water are dimethoate and omethoate.

Table 5.1.4. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression.

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Dimethoate and omethoate	Dimethoate and omethoate
	Rotational Crop	Dimethoate and omethoate	Not Applicable
Livestock	Ruminant	Dimethoate and omethoate	Dimethoate and omethoate
	Poultry	Dimethoate and omethoate	Dimethoate and omethoate
Drinking Water		Dimethoate and omethoate	Not Applicable

Toxicological studies have been submitted for several dimethoate metabolites, including omethoate, hydroxy dimethoate, O-desmethyl omethoate carboxylic acid, des-o-methyl isodimethoate, O-desmethyl omethoate, and dimethoate carboxylic acid. Omethoate was the only metabolite that demonstrated significant inhibition of AChE and is thus the only metabolite of concern.

5.2 Food Residue Profile

HED has previously evaluated residue data depicting the magnitude of dimethoate residues of concern in/on all registered crops. Quantifiable residues were found in crops with short pre-harvest intervals (PHIs; e.g., celery, beans, citrus), resulting in tolerance levels of up to 5.0 ppm in food commodities. Dimethoate was generally the major component of the total residue.

Extensive USDA PDP monitoring data for residues of dimethoate and omethoate in numerous commodities are available. The PDP was specifically designed for risk assessment; analysts prepare samples in a manner similar to typical consumer practices, such as washing, coring/pitting, and/or peeling. The PDP samples are collected at large-scale distribution centers, just prior to sale in grocery stores, and are more likely to reflect "dinner plate" residues. Previous dietary assessments for dimethoate have used FDA surveillance data; however, these data are considerably older than the available PDP data, and were not used in this assessment. Dimethoate and/or omethoate residues were detected by PDP in the following commodities/processed foods with registered tolerances: potatoes without peel (2 detects/1544 samples); leaf lettuce (7 detects/782 samples); celery (253 detects/1480 samples); broccoli (40 detects/1400 samples); cauliflower (9 detects/923 samples); kale (13 detects/802 samples); fresh green beans (84 detects/1480 samples); canned green beans (1 detect/928 samples); frozen green beans (8 detects/555 samples); fresh snap peas (420 detects/1487 samples); frozen sweet peas (90 detects/744 samples); fresh tomatoes (6 detects/1481 samples); canned tomatoes (1 detect/737 samples); bell peppers (80 detects/1671 samples); non-bell peppers (90 detects/739 samples); cantaloupes (19 detects/1482 samples); watermelons (15 detects/371 samples); tangerines (2 detects/1426 samples); pears (3 detects/1485 samples); cherries (1 detect/419 samples); blueberries (10 detects/1477 samples); and fresh asparagus (2 detects/1488 samples).

HED has evaluated residue data pertaining to the potential for concentration of dimethoate residues of concern in processed commodities. Significant concentration of residues was seen only in dried citrus pulp. PDP data are available for the following processed foods: tomato paste, canned tomatoes, orange juice, canned black, kidney, pinto, and garbanzo beans, canned peas, canned pears, and green bean, pea, and pear baby food. Residues of dimethoate and/or omethoate were not detected in any sample, except as outlined above.

5.3 Water Residue Profile

The residues of concern in drinking water for purposes of risk assessment are dimethoate and omethoate. EFED provided estimated drinking water concentrations (EDWCs) in the following drinking water assessment: "Tier II Drinking Water Assessment for Dimethoate for the Use in Human Health Risk Assessment in the Registration Review Risk Assessment (J. Meléndez, 28-JUL-2014; D415002). The EDWCs were calculated using the Tier II Surface Water Concentration Calculator (SWCC), the Tier II Pesticide Root Zone Model-Groundwater (PRZM-GW), and the Tier I Screening Concentration in Ground Water (SCI-GROW) models; however, dietary assessments were not completed using groundwater values since the peak EDWCs for groundwater were substantially lower than those for surface waters. Groundwater values and characterization are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

Surface water runs were initially performed at the maximum application rate and number of applications, minimum reapplication interval, and default national percent cropped area (PCA; equal to 0.91 or 91% for agricultural crops and 1.0 or 100% for non-agricultural uses) using the Tier II SWCC model. Preliminary dietary exposure assessments indicated that the maximum application rate EDWCs resulted in dietary exposure estimates that were above the LOC for many scenarios. Therefore, modeling with typical application rates and regional PCA for agricultural uses was conducted to provide typical rate EDWCs for dietary assessments. No

typical usage data were available for the non-agricultural uses; therefore, typical non-agricultural scenarios were modeled with lower rates using a set of assumptions that are discussed in the most recent drinking water memo (J. Meléndez, 28-JUL-2014; D415002).

Daily time-series outputs that simulate 29 years (1962-1990) of residues of dimethoate in surface drinking water for the 44 different scenarios were modeled using the Tier II SWCC. These scenarios were selected based on the use rates and encompass both maximum (24 scenarios) and typical (20 scenarios) application rates for agricultural and non-agricultural uses of dimethoate. Additional details regarding the selection of the scenarios can be found in the most recent drinking water memo (J. Meléndez, 28-JUL-2014; D415002). Since omethoate was not observed in the environmental fate studies in significant amounts, the omethoate equivalent values were expressed based on its toxicity relative to dimethoate. All of the time-series data were adjusted to reflect 100% conversion of dimethoate to omethoate[8] by multiplying the residues by the acute (8X) and steady-state (3X) TAFs. Therefore, EFED provided a total of 88 distributions: 44 distributions that were adjusted using the acute TAF ("acute distributions") and 44 distributions that were adjusted using the steady-state TAF ("steady-state distributions"). No further adjustments were made to the acute distribution files. Since the steady-state average dietary assessments used 21-day rolling averages for drinking water, the steady-state distributions were further adjusted to be 21-day rolling averages. In the 21-day rolling average distributions, the first data point is the average of days 1-21, the second data point is the average of days 2-22, the third data point is the average of days 3-23, etc. The 21-day rolling average continues until the last 20 days of residues of the final distribution year (1990). For these residues, the average was taken only of the remaining days, resulting in residue values that are not 21-day averages.

Summary tables for EDWCs using maximum and typical application rates can be found in Appendix H.

5.4 Dietary Risk Assessment

Highly refined acute and steady-state (two-day average) dietary exposure and risk assessments for dimethoate and its metabolite omethoate were conducted using DEEM-FCID Version 3.18. This model uses 2003-2008 food consumption data from USDA's NHANES/WWEIA. Acute and steady-state assessments were conducted for food only, drinking water only, and for food and drinking water. When a drinking water only assessment resulted in a risk of concern at the 99.9th percentile, a food and drinking water assessment was not conducted for that drinking water scenario since the combined assessment would also result in risks of concern at the 99.9th percentile.

5.4.1 Overview of Residue Data Used

The residue chemistry database is adequate to support current Registration Review requirements. Both the acute and steady-state assessments were refined using distributions and point estimates derived from PDP monitoring data, PCT data, empirical and default processing factors, and cooking factors derived from literature studies. If monitoring data were not available for a particular commodity (i.e., mung beans), but were available for a similar commodity (i.e., black

[8] MRID 48041103 - Marin, J.E. 2010. Determination of the effect of chlorination on the degradation of dimethoate in water.

beans), the available data were translated to the similar crop. HED SOP 99.3, HED SOP 2000.1, and use pattern information were used as guidance for translations. When data were translated, the residue distribution file (RDF) was adjusted to account for differences in PCT. All RDFs were adjusted to account for the acute (8X) and steady-state (3X) omethoate TAFs. Tolerance-level values were used for pecan, sorghum, safflower, and cottonseed since monitoring data were not available for these commodities. HED previously recommended that tolerances for residues of dimethoate and omethoate in/on egg and poultry meat byproducts should be revoked (M. Sahafeyan D232849; 24-MAY-2011); however, the 40 CFR still includes tolerances for these commodities. Egg and poultry meat byproduct PDP data were included in the assessments as a conservative assumption.

The most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590) summarizes the residue inputs (RDFs used, point estimates, processing and cooking factors, PCT, etc.), empirical processing factor calculations, residue data used for each commodity, procedures for combining residues of dimethoate and omethoate, and all of the RDF files used for the acute and steady-state assessments.

5.4.2 Percent Crop Treated Used in Dietary Assessment

The acute and steady-state analyses incorporated maximum PCT data provided by BEAD for the following commodities: alfalfa (<2.5%); asparagus (5%); beans, green (20%); broccoli (55%); cantaloupes (10%); cauliflower (45%); celery (35%); cherry (15%); corn (<2.5%); cotton (<2.5%); dry beans/peas (10%); grapefruit (15%); lemons (20%); lettuce (35%); oranges (25%); pears (<2.5%); peas, green (25%); pecan (5%); peppers (25%); potatoes (15%); sorghum (<2.5%); soybeans (<2.5%); tangerines (5%); tomatoes (40%); watermelons (10%); and wheat (<2.5%).

5.4.3 Acute Dietary Risk Assessment

The food only acute dietary risk estimates are summarized in Table 5.4.6.1 and are above HED's LOC (>100% of the aPAD) for the U.S. population and all population subgroups at the 99.9th percentile. The U.S. population was 270% of the aPAD and children 1-2 years old, the most highly exposed population subgroup, was 640% of the aPAD. For the acute drinking water only runs, all (24) of the maximum application rate and 19 of the typical application rate drinking water scenarios resulted in risks of concern at the 99.9th percentile.

Since the food alone and drinking water alone assessments result in risks of concern, acute food and drinking water analyses were not completed for all of the scenarios since they would also result in risks of concern at the 99.9th percentile. Overall, acute food and drinking water analyses were conducted for the 27 (7 maximum application rate and 20 typical application rate) drinking water scenarios and are summarized in Tables 5.4.6.3 and 5.4.6.4 for the most highly exposed population subgroups. Infants and children 1-2 years old were the most highly exposed population subgroups for these scenarios, with risk estimates that ranged from 710-1100% of the aPAD and 640-680% of the aPAD at the 99.9th percentile, respectively. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

5.4.4 Steady-State Dietary Risk Assessment

The food only steady-state results are summarized in Table 5.4.6.2 and are above HED's LOC (>100% of the ssPAD) for the U.S. population and all population subgroups at the 99.9th percentile. The U.S. population was 410% of the ssPAD and children 1-2 years old, the most highly exposed population subgroup, was 810% of the ssPAD. For the steady-state drinking water only analyses, all (24) of the maximum application rate and 19 of the typical application rate drinking water scenarios resulted in risks of concern at the 99.9th percentile.

Since the food alone and drinking water alone assessments result in risks of concern, steady-state food and drinking water analyses were not completed for all of the scenarios since they would also result in risks of concern at the 99.9th percentile. Overall, food and drinking water steady-state analyses were conducted for 23 drinking water scenarios (3 maximum application rate and 20 typical application rate) and are summarized in Tables 5.4.6.5 and 5.4.6.6 for the most highly exposed population subgroups. Infants and children 1-2 years old were the most highly exposed population subgroups for these scenarios, with risk estimates that ranged from 970-1200% of the ssPAD and 810-880% of the ssPAD at the 99.9th percentile, respectively. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590)

5.4.5 Cancer Dietary Risk Assessment

Dimethoate is classified as a Group C carcinogen (possible human carcinogen). Quantification of risk using a non-linear approach will adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

5.4.6. Dietary Assessment Summary Tables

Table 5.4.6.1. Summary of Acute Dietary (Food Only) Exposure and Risk for Dimethoate and Omethoate[1].

Population Subgroup	aPAD (mkd)[2]	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD
General U.S. Population	0.00091	0.000630	69	0.001192	130	0.002501	270
All Infants (<1 year old)		0.000933	100	0.001668	180	0.002506	280
Children 1-2 years old		0.001691	190	0.002912	320	**0.005779**	**640**
Children 3-5 years old		0.001267	140	0.002226	240	0.005053	560
Children 6-12 years old		0.000762	84	0.001394	150	0.002811	310
Youth 13-19 years old		0.000452	50	0.000929	100	0.001683	180
Adults 20-49 years old		0.000391	43	0.000735	81	0.001447	160
Adults 50-99 years old		0.000370	4.1	0.000652	7.2	0.001346	15
Females 13-49 years old		0.000380	42	0.000758	83	0.001399	150

Residue file: Dimethoate Acute File December 19 2014__FOOD ONLY.R08; Residue file dated: 12-19-2014/16:47:51

[1] Population with the greatest exposure is in bold. The exposure assessment was run using a rounded aPAD value of 0.009 mkd. The %aPAD values have been updated to reflect the unrounded aPAD value and have been rounded to two significant figures.

[2] mkd = mg/kg/day. Includes 10x FQPA SF for all population subgroups except adults 50-99 years old. The aPAD for adults 50-99 years old is 0.0091 mkd.

Table 5.4.6.2. Summary of Steady-State (Two-Day Average) Dietary (Food Only) Exposure and Risk for Dimethoate and Omethoate[1].

Population Subgroup	ssPAD (mkd)[2]	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD
General U.S. Population	0.00022	0.000276	130	0.000493	220	0.000909	410
All Infants (<1 year old)		0.000410	190	0.000670	300	0.000974	440
Children 1-2 years old		0.000706	320	0.001022	460	**0.001775**	**810**
Children 3-5 years old		0.000516	230	0.000772	350	0.001465	670
Children 6-12 years old		0.000331	150	0.000496	230	0.000964	440
Youth 13-19 years old		0.000196	89	0.000302	140	0.000508	230
Adults 20-49 years old		0.000159	72	0.000255	120	0.000475	220
Adults 50-99 years old		0.000145	6.6	0.000231	11	0.000435	20
Females 13-49 years old		0.000158	72	0.000259	120	0.000458	210

Residue file: Dimethoate Steady-state File December 30 2014__FOOD ONLY_ssRfD.R08; Residue file dated: 12-30-2014/10:45:39

[1] Population with the greatest exposure is in bold. The exposure assessment was run using the rounded ssPAD value of 0.002 mkd. The %ssPAD values have been updated to reflect the unrounded ssPAD value and have been rounded to two significant figures.

[2] mkd = mg/kg/day. Includes 10x FQPA SF for all population subgroups except adults 50-99 years old. The ssPAD for adults 50-99 years old is 0.0022 mkd.

Table 5.4.6.3. Summary of Acute Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD		Exposure (mkd)	% aPAD
01_CA wine grapes/ Agricultural uncultivated areas (CA only) (Noncropland adjacent to vineyards)	0.003130	340	0.047486	5200	0.001596	180	0.023139	2500	N/C	N/C	N/C
03_MN alfalfa/ Alfalfa, Sainfoin	0.002260	250	0.012488	1400	0.001083	120	0.006579	720	N/C	N/C	N/C
04_CA cole crops/ Broccoli, Cauliflower; Additionally, Brussels sprouts (aerial, some labels allow use only in CA)	0.004635	510	0.028422	3100	0.002352	260	0.015074	1700	N/C	N/C	N/C
06_CA row crops/ Celery	0.001555	170	0.008732	960	**0.000760**	**84**	0.004674	510	All Infants (<1 year old)	0.008981	990
07_FL cabbage/ Turnip (greens)	0.002608	290	0.016004	1800	0.001328	150	0.008751	960	N/C	N/C	N/C
08_CA potato/ Turnip (roots)	0.002330	260	0.012046	1300	0.001178	130	0.006658	730	N/C	N/C	N/C
09_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.002461	270	0.009575	1100	0.001173	130	0.005499	600	All Infants (<1 year old)	0.009749	1100
10_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.002797	310	0.009974	1100	0.001303	140	0.005854	640	All Infants (<1 year old)	0.010227	1100
12_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	0.002453	270	0.013023	1400	0.001266	140	0.007147	790	N/C	N/C	N/C
13_CA forestry/ Cottonwood (forest/ shelterbelt)	0.009973	1100	0.036147	4000	0.004655	510	0.021136	2300	N/C	N/C	N/C

Table 5.4.6.3. Summary of Acute Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD		Exposure (mkd)	% aPAD
18_NJ nursery/ Ornamental herbaceous plants[1]	0.007523	830	0.096285	11000	0.004324	480	0.048787	5400	N/C	N/C	N/C
20_FL peppers/ Peppers	0.002748	300	0.034351	3800	0.001500	160	0.017000	1900	N/C	N/C	N/C
21_FL peppers/ Peppers	0.002044	220	0.033765	3700	0.001176	130	0.016433	1800	N/C	N/C	N/C
22_MI beans/ Beans (includes dry beans, excludes cowpeas), Garbanzos (includes chick peas), Lupine	0.001478	160	0.009937	1100	**0.000744**	**82**	0.005244	580	All Infants (<1 year old)	0.010354	1100
24_PA Tomato/ Tomato	0.001825	200	0.032938	3600	0.000936	100	0.015693	1700	N/C	N/C	N/C
25_CA citrus/ Grapefruit, Kumquat, Lemon, Lime, Orange, Pummelo (shaddock), Tangelo, Tangerine	**0.000889**	**98**	0.006597	720	**0.000513**	**56**	0.003575	390	All Infants (<1 year old)	0.006881	760
26_FL citrus/ Same crops as above	0.001208	130	0.025690	2800	**0.000759**	**83**	0.012608	1400	N/C	N/C	N/C
27_ID potatoes/ Potatoes	0.003140	350	0.015391	1700	0.001564	170	0.008542	940	N/C	N/C	N/C
05_CA cole crops/ Brussels sprouts (ground)	0.003661	400	0.044642	4900	0.002022	220	0.022424	2500	N/C	N/C	N/C
14_OR Xmas trees/ Hybrid cottonwood/poplar plantations (some labels allow use in ID, OR and WA)	0.009177	1000	0.037244	4100	0.004391	480	0.021056	2300	N/C	N/C	N/C

Table 5.4.6.3. Summary of Acute Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD		Exposure (mkd)	% aPAD
10b_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.001378	150	0.004921	540	**0.000642**	**71**	0.002894	320	Children 1-2 years old	0.006152	680
15_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	0.001228	130	0.006874	760	**0.000645**	**71**	0.00378	420	All Infants (<1 year old)	0.007164	790
23_MS Cotton/ Cotton	0.001079	120	0.012753	1400	**0.000601**	**66**	0.006364	700	N/C	N/C	N/C
17_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	0.005901	650	0.023714	2600	0.002798	310	0.013584	1500	N/C	N/C	N/C

Bold and shaded values are <100% of the aPAD. N/C = not calculated. Since the food alone and drinking water alone assessments result in risks of concern, acute food and drinking water analyses were not completed for the majority of the scenarios since they would also result in risks of concern at the 99.9th percentile. Food and drinking water exposure assessments were conducted for a subset of drinking water scenarios as an example of the combined dietary exposures and risks even though food alone and water alone resulted in risks of concern. The exposure assessments were run using a rounded aPAD value of 0.009 mkd. The %aPAD values have been updated to reflect the unrounded aPAD value of 0.00091 mkd and were adjusted to two significant figures. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

[1] A maximum rate of 6.5 lb ai/A for this use appears to be a label error; therefore, these results are not considered representative. A drinking water only assessment was completed using this distributions since the label has not yet been modified.

Table 5.4.6.4. Summary of Acute Assessment Results for Typical Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD		Exposure (mkd)	% aPAD
03c_MN alfalfa/ Alfalfa	**0.000444**	**49**	0.003749	410	**0.000231**	**25**	0.001913	210	Children 1-2 years old	0.005846	640
04b_CA cole crops/ Broccoli	**0.000773**	**85**	0.007920	870	**0.000409**	**45**	0.004006	440	All Infants (<1 year old)	0.008169	900

Table 5.4.6.4. Summary of Acute Assessment Results for Typical Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th			99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Population Subgroup	Exposure (mkd)	% aPAD
17b_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	**0.000368**	**40**	0.002475	270	**0.000194**	**21**	0.001305	140	Children 1-2 years old	0.005798	640
18b_NJ nursery/ Ornamental herbaceous plants	**0.000281**	**31**	0.003593	390	**0.000161**	**18**	0.001820	200	Children 1-2 years old	0.005836	640
22c_MI beans/ Dry beans, peas	**0.000350**	**38**	0.004195	460	**0.000194**	**21**	0.002109	230	Children 1-2 years old	0.005875	650
23c_MS Cotton/ Cotton	**0.000171**	**19**	0.003917	430	**0.000109**	**12**	0.001907	210	Children 1-2 years old	0.005835	640
24b_PA Tomato/ Tomato	**0.000187**	**21**	0.002325	260	**0.000098**	**11**	0.001128	120	Children 1-2 years old	0.005831	640
26b_FL citrus/ Oranges	**0.000226**	**25**	0.005462	600	**0.000141**	**15**	0.002659	290	Children 1-2 years old	0.005987	660
27c_ID potatoes/ Potatoes	0.001333	150	0.006605	730	**0.000665**	**73**	0.003655	400	All Infants (<1 year old)	0.006905	760
27d_ID potatoes/ Potatoes	**0.000629**	**69**	0.003762	410	**0.000328**	**36**	0.002042	220	Children 1-2 years old	0.005869	640
28_IL corn/ Corn	**0.000451**	**50**	0.007578	830	**0.000243**	**27**	0.003537	390	All Infants (<1 year old)	0.007916	870
29_KS sorghum/ Sorghum	**0.000267**	**29**	0.006286	690	**0.000151**	**17**	0.003154	350	All Infants (<1 year old)	0.006488	710
30_MS soybeans/ Soybeans	**0.000282**	**31**	0.003531	390	**0.000167**	**18**	0.001744	190	Children 1-2 years old	0.00584	640
31_OR snap beans/ Lima beans	**0.000547**	**60**	0.002682	290	**0.000272**	**30**	0.001503	170	Children 1-2 years old	0.005807	640
32_ND wheat/ Spring wheat	**0.000205**	**23**	0.001274	140	**0.000112**	**12**	**0.000700**	**77**	Children 1-2 years old	0.005815	640
33_ND wheat/ Winter wheat	**0.000255**	**28**	0.001587	170	**0.000139**	**15**	**0.000872**	**96**	Children 1-2 years old	0.005788	640
13b_CA forestry/ Cottonwood (forest/ shelterbelt)	0.001209	130	0.006982	770	**0.000610**	**67**	0.003794	420	All Infants (<1 year old)	0.007370	810
14b_OR Xmas trees/ Hybrid cottonwood/poplar	0.001083	120	0.005602	620	**0.000558**	**61**	0.003099	340	Children 1-2 years old	0.006109	670

Table 5.4.6.4. Summary of Acute Assessment Results for Typical Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% aPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Acute WATER ONLY (All Infants <1 year old)				Acute WATER ONLY (Children 1-2 years old)				Acute FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD	Exposure (mkd)	% aPAD		Exposure (mkd)	% aPAD
plantations (some labels allow use in ID, OR and WA)											
15b_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	**0.000108**	**12**	**0.000604**	**66**	**0.000057**	**6.3**	**0.000332**	**36**	Children 1-2 years old	0.00578	640
12b_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	**0.000546**	**60**	0.002896	320	**0.000282**	**31**	0.00159	170	Children 1-2 years old	0.005807	640

Bold and shaded values are <100% of the aPAD. N/C = not calculated. The exposure assessments were run using a rounded aPAD value of 0.009 mkd. The %aPAD values have been updated to reflect the unrounded aPAD value of 0.00091 mkd and were adjusted to two significant figures. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

Table 5.4.6.5. Summary of Steady-State (Two-Day Average) Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% ssPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Two-Day Average WATER ONLY (All Infants <1 year old)				Two-Day Average WATER ONLY (Children 1-2 years old)				Two-Day Average FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD		Exposure (mkd)	% ssPAD
01_CA wine grapes/ Agricultural uncultivated areas (CA only) (Noncropland adjacent to vineyards)	0.001087	490	0.016100	7300	0.000562	260	0.007729	3500	N/C	N/C	N/C
03_MN alfalfa/ Alfalfa, Sainfoin	0.000818	370	0.004016	1800	0.000392	180	0.002055	930	N/C	N/C	N/C
04_CA cole crops/ Broccoli, Cauliflower; Additionally, Brussels sprouts (aerial, some	0.001730	790	0.009069	4100	0.000872	400	0.004692	2100	N/C	N/C	N/C

Table 5.4.6.5. Summary of Steady-State (Two-Day Average) Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% ssPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Two-Day Average WATER ONLY (All Infants <1 year old)				Two-Day Average WATER ONLY (Children 1-2 years old)				Two-Day Average FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD		Exposure (mkd)	% ssPAD
labels allow use only in CA)											
06_CA row crops/ Celery	0.000570	260	0.002854	1300	0.000279	130	0.001469	670	N/C	N/C	N/C
07_FL cabbage/ Turnip (greens)	0.000976	440	0.005096	2300	0.000501	230	0.002641	1200	N/C	N/C	N/C
08_CA potato/ Turnip (roots)	0.000871	400	0.003973	1800	0.000432	200	0.002099	950	N/C	N/C	N/C
09_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.000888	400	0.002903	1300	0.000415	190	0.001652	750	N/C	N/C	N/C
10_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.000993	450	0.003111	1400	0.000465	210	0.001773	810	N/C	N/C	N/C
12_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	0.000940	430	0.003944	1800	0.000456	210	0.002166	980	N/C	N/C	N/C
13_CA forestry/ Cottonwood (forest/ shelterbelt)	0.003578	1600	0.011923	5400	0.001671	760	0.006713	3100	N/C	N/C	N/C
18_NJ nursery/ Ornamental herbaceous plants[1]	0.003069	1400	0.029122	13000	0.001702	770	0.014279	6500	N/C	N/C	N/C
20_FL peppers/ Peppers	0.001110	500	0.010331	4700	0.000591	270	0.005063	2300	N/C	N/C	N/C
21_FL peppers/ Peppers	0.000859	390	0.010034	4600	0.000478	220	0.004894	2200	N/C	N/C	N/C
22_MI beans/ Beans (includes dry beans, excludes cowpeas), Garbanzos (includes chick peas), Lupine	0.000545	250	0.003227	1500	0.000276	130	0.001625	740	N/C	N/C	N/C

Table 5.4.6.5. Summary of Steady-State (Two-Day Average) Assessment Results for Maximum Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% ssPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Two-Day Average WATER ONLY (All Infants <1 year old)				Two-Day Average WATER ONLY (Children 1-2 years old)				Two-Day Average FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD		Exposure (mkd)	% ssPAD
24_PA Tomato/ Tomato	0.000675	310	0.011389	5200	0.000348	160	0.005484	2500	N/C	N/C	N/C
25_CA citrus/ Grapefruit, Kumquat, Lemon, Lime, Orange, Pummelo (shaddock), Tangelo, Tangerine	0.000381	170	0.001826	830	**0.000194**	**88**	0.000975	440	Children 1-2 years old	0.001929	880
26_FL citrus/ Same crops as above	0.000551	250	0.007940	3600	0.000307	140	0.003761	1700	N/C	N/C	N/C
27_ID potatoes/ Potatoes	0.001161	530	0.004764	2200	0.000568	260	0.002548	1200	N/C	N/C	N/C
05_CA cole crops/ Brussels sprouts (ground)	0.001412	640	0.014579	6600	0.000776	350	0.007200	3300	N/C	N/C	N/C
14_OR Xmas trees/ Hybrid cottonwood/poplar plantations (some labels allow use in ID, OR and WA)	0.003320	1500	0.011918	5400	0.001574	720	0.006844	3100	N/C	N/C	N/C
10b_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	0.000489	220	0.001542	700	0.000229	100	0.000877	400	Children 1-2 years old	0.001913	870
15_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	0.000481	220	0.001987	900	0.000235	110	0.001081	490	All Infants (<1 year old)	0.002124	970
23_MS Cotton/ Cotton	0.000433	200	0.004079	1900	0.000234	110	0.002005	910	N/C	N/C	N/C
17_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	0.002123	970	0.007785	3500	0.001009	460	0.004241	1900	N/C	N/C	N/C

Bold and shaded values are <100% of the ssPAD. N/C = not calculated. Since the food alone and drinking water alone assessments result in risks of concern, steady-state (two-day average) food and drinking water analyses were not completed for the majority of the scenarios since they would also result in risks of concern at the 99.9th percentile. Food and drinking water exposure assessments were conducted for a subset of drinking water scenarios as an example of the combined dietary exposures and risks even though food alone and water alone resulted in risks of concern. The exposure assessments were run using a rounded ssPAD value of 0.002 mkd. The %ssPAD values have been updated to reflect the unrounded ssPAD value of 0.00022 mkd and were adjusted to two significant figures. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

Table 5.4.6.6. Summary of Steady-State (Two-Day Average) Assessment Results for Typical Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% ssPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Two-Day Average WATER ONLY (All Infants <1 year old)				Two-Day Average WATER ONLY (Children 1-2 years old)				Two-Day Average FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th			99.9th	
	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Population Subgroup	Exposure (mkd)	% ssPAD
03c_MN alfalfa/ Alfalfa	**0.000170**	**77**	0.001220	550	**0.000085**	**39**	0.000591	270	Children 1-2 years old	0.001802	820
04b_CA cole crops/ Broccoli	0.000291	130	0.002549	1200	**0.000153**	**70**	0.001241	560	All Infants (<1 year old)	0.002687	1200
17b_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	**0.000142**	**65**	0.000761	350	**0.000071**	**32**	0.000396	180	Children 1-2 years old	0.001792	810
18b_NJ nursery/ Ornamental herbaceous plants	**0.000114**	**52**	0.001087	490	**0.000064**	**29**	0.000533	240	Children 1-2 years old	0.001792	810
22c_MI beans/ Dry beans, peas	**0.000141**	**64**	0.001328	600	**0.000074**	**34**	0.00064	290	Children 1-2 years old	0.001805	820
23c_MS Cotton/ Cotton	**0.000081**	**37**	0.00117	530	**0.000046**	**21**	0.000566	260	Children 1-2 years old	0.001790	810
24b_PA Tomato/ Tomato	**0.000071**	**32**	0.000787	360	**0.000036**	**16**	0.000385	180	Children 1-2 years old	0.001789	810
26b_FL citrus/ Oranges	**0.000101**	**46**	0.001687	770	**0.000057**	**26**	0.000797	360	Children 1-2 years old	0.001821	830
27c_ID potatoes/ Potatoes	0.000494	220	0.002050	930	0.000242	110	0.001092	500	All Infants (<1 year old)	0.002183	990
27d_ID potatoes/ Potatoes	0.000244	110	0.001088	490	**0.000121**	**55**	0.000571	260	Children 1-2 years old	0.001810	820

Table 5.4.6.6. Summary of Steady-State (Two-Day Average) Assessment Results for Typical Application Rate Drinking Water Scenarios (Water Only: 95th and 99.9th Percentiles; Food+Water: 99.9th Percentile). (Values <100% ssPAD are Shaded and in Bold.)

Drinking Water Scenario (bold font)/ Crops/Uses Represented	Two-Day Average WATER ONLY (All Infants <1 year old)				Two-Day Average WATER ONLY (Children 1-2 years old)				Two-Day Average FOOD and WATER Highest Exposure Estimate		
	95th		99.9th		95th		99.9th		Population Subgroup	99.9th	
	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD	Exposure (mkd)	% ssPAD		Exposure (mkd)	% ssPAD
28_IL corn/ Corn	**0.000169**	**77**	0.002382	1100	**0.000092**	**42**	0.001147	520	All Infants (<1 year old)	0.002480	1100
29_KS sorghum/ Sorghum	**0.000108**	**49**	0.002212	1000	**0.000058**	**26**	0.001033	470	All Infants (<1 year old)	0.002362	1100
30_MS soybeans/ Soybeans	**0.000122**	**55**	0.00103	470	**0.000066**	**30**	0.000517	240	Children 1-2 years old	0.001793	820
31_OR snap beans/ Lima beans	**0.000202**	**92**	0.000825	380	**0.000099**	**45**	0.000458	210	Children 1-2 years old	0.001794	820
32_ND wheat/ Spring wheat	**0.000082**	**37**	0.000381	170	**0.000041**	**19**	**0.000202**	**92**	Children 1-2 years old	0.001786	810
33_ND wheat/ Winter wheat	**0.000102**	**46**	0.000474	220	**0.000051**	**23**	0.000252	110	Children 1-2 years old	0.001787	810
13b_CA forestry/ Cottonwood (forest/ shelterbelt)	0.000455	210	0.002198	1000	0.000219	100	0.001155	530	All Infants (<1 year old)	0.002338	1100
14b_OR Xmas trees/ Hybrid cottonwood/poplar plantations (some labels allow use in ID, OR and WA)	0.000415	190	0.001671	760	**0.000201**	**91**	0.000912	410	Children 1-2 years old	0.001909	870
15b_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	**0.000042**	**19**	**0.000175**	**80**	**0.000021**	**10**	**0.000095**	**43**	Children 1-2 years old	0.001777	810
12b_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	**0.000209**	**95**	0.000877	400	**0.000101**	**46**	0.000482	220	Children 1-2 years old	0.001796	820

Bold and shaded values are ≤100% of the ssPAD. The exposure assessments were run using a rounded ssPAD value of 0.002 mkd. The %ssPAD values have been updated to reflect the unrounded ssPAD value of 0.00022 mkd and were adjusted to two significant figures. The results for all population subgroups (general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50-99 years) for all runs are summarized in the most recent dietary memo (J. Van Alstine; 15-SEP-2015; D418590).

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

All residential and other non-occupational uses of dimethoate were voluntarily cancelled, effective March 13, 2002.[9] Currently, dimethoate is registered solely for use on occupational sites.

6.1 Residential Handler Exposure

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. There are currently no registered or proposed residential uses for dimethoate; therefore, a residential handler assessment was not performed.

6.2 Post-Application Exposure

There are currently no registered or proposed residential uses for dimethoate. The potential for non-occupational post-application exposure from agricultural applications of dimethoate has been assessed below in Section 8.0.

7.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its FIFRA SAP in December 2009, and received the SAP's final report on March 2, 2010.[10] The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis.[11] During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies) or further analyses are required for dimethoate.

8.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Off-target movement of pesticides can occur via many types of pathways and it is governed by a variety of factors. Sprays that are released and do not deposit in the application area end up off-target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to indirect exposures (e.g., children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling onto 50-feet-wide lawns coupled with methods employed for residential risk assessments for turf products.

The approach to be used for quantitatively incorporating spray drift into risk assessment is based on a premise of compliant applications that, by definition, should not result in direct exposures to individuals because of existing label language and other regulatory requirements intended to prevent them.[12] Direct exposures would include inhalation of the spray plume or being sprayed directly. Rather, the exposures addressed here are thought to occur indirectly through contact

[9] Federal Register Notice/Vol. 67, No. 84/Wednesday, May 01, 2002/Notices/21669
[10] http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html
[11] http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219
[12] This approach is consistent with the requirements of the EPA's Worker Protection Standard.

with impacted areas, such as residential lawns, when compliant applications are conducted. Given this premise, exposures for children (1 to 2 years old) and adults who have contact with turf where residues are assumed to have deposited via spray drift thus resulting in an indirect exposure are the focus of this analysis analogous to how exposures to turf products are considered in risk assessment.

In order to evaluate the drift potential and associated risks, an approach based on drift modeling coupled with techniques used to evaluate residential uses of pesticides was utilized. Essentially, a residential turf assessment based on exposure to deposited residues has been completed to address drift from the agricultural applications of dimethoate. In the spray drift scenario, the deposited residue value was determined based on the amount of spray drift that may occur at varying distances from the edge of the treated field using the AgDrift® (v2.1.1) model and the *Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift Policy*. Once the deposited residue values were determined, the remainder of the spray drift assessment was based on the algorithms and input values specified in the recently revised (2012) *Standard Operating Procedures For Residential Risk Assessment (SOPs)*.

For dimethoate, chemical-specific turf transferrable residue (TTR) data are not available, therefore, the estimated TTR are based on a default assumption from the 2012 Residential SOPs that the transferable residue available for exposure is 1% of the total deposited residue, which is assumed to be equivalent to the maximum application rate. In order to account for the formation of the metabolite, omethoate, an assumption was made that 5% of the dimethoate residues would metabolize to omethoate. This assumption is based on a review of available TTR and DFR data for other OPs where both the parent and metabolite were measured in residue samples. Five percent was found to be the high-end value for the percent of parent that metabolized during the course of the residue studies. Once the estimated omethoate residues were calculated (dimethoate residues x 5%), the resulting values were adjusted further by the steady-state TAF value of 3 to account for the increased potency of omethoate since a dimethoate-specific dermal toxicity study was used for calculation of the risk estimates.

A screening approach was developed based on the use of the AgDrift® model in situations where specific label guidance that defines application parameters is not available.[13] AgDrift® is appropriate for use only when applications are made by aircraft, airblast orchard sprayers, and groundboom sprayers. When AgDrift® was developed, a series of screening values (i.e., the Tier 1 option) were incorporated into the model and represent each equipment type and use under varied conditions. The screening options specifically recommended in this methodology were selected because they are plausible and represent a reasonable upper bound level of drift for common application methods in agriculture. These screening options are consistent with how spray drift is considered in a number of ecological risk assessments and in the process used to develop drinking water concentrations used for risk assessment. In all cases, each scenario is to be evaluated unless it is not plausible based on the anticipated use pattern (e.g., herbicides are not typically applied to tree canopies) or specific label prohibitions (e.g., aerial applications are not allowed). Section 8.1 provides the screening-level drift-related risk estimates. In many cases, risks are of concern when the screening-level estimates for spray drift are used as the basis for the analysis. In order to account for this issue and to provide additional risk management

[13]http://www.agdrift.com/

options, additional spray drift deposition fractions were also considered. These drift estimates represent plausible options for pesticide labels.

8.1 Combined Risk Estimates from Lawn Deposition Adjacent to Applications

The spray drift risk estimates are based on an estimated deposited residue concentration as a result of the screening level agricultural application scenarios. Dimethoate is registered on various agricultural crops, Christmas tree farms, trees grown for pulp, and ornamentals in outdoor nurseries. Most of the registered products are applied either via aerial, chemigation, groundboom, airblast or with handheld equipment. For most use sites, the maximum application rate is 2 lb ai/A, but for ornamentals in outdoor nurseries, the maximum application rate is 4.15 lb ai/A for airblast applications specifically. The recommended drift scenario screening level options are listed below:

- **Groundboom applications** are based on the AgDrift® option for high boom height and using very fine to fine spray type using the 90th percentile results.
- **Orchard airblast applications** are based on the AgDrift® option for sparse (young/dormant) tree canopies.
- **Aerial applications** are based on the use of AgDrift® Tier 1 aerial option for a fine to medium spray type and a series of other parameters that will be described in more detail below (e.g., wind vector assumed to be 10 mph in a downwind direction for entire application/drift event).[14]

In addition to the screening-level spray-drift scenarios described above, additional results are provided which represent viable drift-reduction options that represent potential risk-management options. In particular, different spray qualities have been considered as well as the impact of other application conditions (e.g., boom height, use of a helicopter instead of fixed-wing aircraft, crop canopy conditions).

Dermal risk estimates were calculated for adults. For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, brain AChE inhibition, is not sex-specific, the female-specific body weight was used to protect for pregnant women due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4). Dermal and incidental oral risk estimates for children (1 to <2 years old) were combined because the toxicity endpoint for each route of exposure is same (i.e., inhibition of brain AChE). The total applicable LOC is 1000, therefore MOEs < 1000 represent risk estimates of concern.

Adult dermal and children's (1 to < 2 year old) dermal and incidental oral risk estimates related to spray drift exceed HED's LOC (MOEs < 1000) at a range of distances from the edge of the field depending on the spray drift scenario. These are summarized in Table 8.1.1. All drift calculations are provided in the most recent ORE memo (K. Lowe; 15-SEP-2015; D418589).

[14] AgDrift® allows for consideration of even finer spray patterns characterized as very fine to fine. However, this spray pattern was not selected as the common screening basis since it is used less commonly for most agriculture. If assessors identify this use pattern it should be used as the screening criteria and deposition values associated with it are provided in Table 1 below. Justification for including this spray quality should be included in any assessment based on specific label directions for its use.

Results indicate that the major risk concern is from aerial applications. Appropriate drift reduction technologies such as changing the spray type/nozzle configuration to coarser spray applications may result in less drift and reduced risk concerns (i.e., higher MOEs) from aerial applications. Similarly, using coarser sprays and lowering boom height for groundboom sprayers reduces risk concerns.

Table 8.1.1. Summary of Spray Drift Buffers for Dimethoate.

Crop Category	Crops	Application rate (lb ai/A)	Adult Buffer Summary			Children 1 < 2 years Buffer Summary (Dermal + Incidental Oral)		
			Buffers Necessary to reach MOE of 1000			Buffers Necessary to reach MOE of 1000		
			Aerial	Groundboom	Airblast	Aerial	Groundboom	Airblast
Forestry	Cottonwoods grown for pulp	2	100 - >300	NA	NA	>300	NA	NA
High Acreage Crops	Alfalfa (field and seed crop), Beans (fresh, snap, lima, dry, not cowpeas), Corn (field and popcorn), Cotton, Grass grown for seed, Potatoes, Safflower, Sorghum, Soybeans, Wheat	0.5	25 - >300	0 - 25		125 - >300	10 -150	
Typical Acreage Crops	Brussels sprouts	1	50 - >300	0 - 50		200 - >300	25 - 250	
	Asparagus, Broccoli, Cauliflower, Celery, Garbanzo beans, Lentils, Melons, Peas, Tomatoes, Watermelon	0.5	10 - >300	0 - 10		125 - >300	10 - 125	
	Peas, dry; Peas, succulent; Peppers	0.33	0 - 200	0 - 10		75 - >300	10 - 75	
	Kale, Mustard greens, Turnip	0.25	0 - 150	0 - 10		75 - >300	10 - 75	
	Peas	0.16	0 - 75	0		50 - >300	0 - 50	
Nurseries / Orchard	Ornamentals in outdoor nurseries	4.15	NA		0 - 100	NA		25 - 250
	Citrus - non-bearing and nursery stock, Cherries (preharvest and postharvest), Christmas tree nurseries, Citrus, Pears (including non-bearing and nursery stock)	1			0 - 25			0 - 100
	Lupine	0.5			0 - 10			0 - 75
Orchard	Pecans	0.33			0 - 10			0 - 50

9.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When

aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. The registered dimethoate uses are not anticipated to result in residential exposure and thus the acute and steady-state dietary exposure estimates provided in Section 5.4.3 and 5.4.4 represent the acute and steady-state aggregate exposure.
Dimethoate is classified as a Group C carcinogen (possible human carcinogen). Quantification of risk using a non-linear approach will adequately account for all chronic toxicity, including carcinogenicity that could result from exposure to dimethoate.

10.0 Cumulative Exposure/Risk Characterization

OPs, like dimethoate/omethoate, share the ability to inhibit AChE through phosphorylation of the serine residue on the enzyme leading to accumulation of acetylcholine and ultimately cholinergic neurotoxicity. This shared MOA/AOP is the basis for the OP common mechanism grouping per OPP's *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999). The 2002 and 2006 CRAs used brain AChE inhibition in female rats as the source of dose response data for the relative potency factors and PODs for each OP, including dimethoate/omethoate. Prior to the completion of Registration Review, OPP will update the OP CRA on AChE inhibition to incorporate new toxicity and exposure information available since 2006.

As described in Section 4.4, OPP has retained the FQPA Safety Factor for OPs, including dimethoate/omethoate, due to uncertainties associated with neurodevelopmental effects in children and exposure to OPs. There is a lack of an established MOA/AOP for the neurodevelopment outcomes which precludes the agency from formally establishing a common mechanism group per the *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999) based on that outcome. Moreover, the lack of a recognized MOA/AOP and other uncertainties with exposure assessment in the epidemiology studies prevent the agency from establishing a causal relationship between OP exposure and neurodevelopmental outcomes. The agency will continue to evaluate the epidemiology studies associated with neurodevelopmental outcomes and OP exposure prior to the release of the revised DRA. During this period, the agency will determine whether or not it is appropriate to apply the draft guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* for the neurodevelopment outcomes.

11.0 Occupational Exposure/Risk Characterization

11.1 Short- and Intermediate-Term Handler Risk

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

For occupational handlers, exposure is anticipated to be to the parent, dimethoate, only. The dermal route of exposure is assessed using a dimethoate-specific toxicity study; therefore, no TAFs were used in the dose calculations. The inhalation route of exposure is assessed using an

omethoate-specific toxicity study since a dimethoate-specific inhalation toxicity study is not available. No TAFs were used in the inhalation dose calculations, but it should be noted that the risk estimates presented are representative of exposure to the more toxic metabolite, omethoate, and, therefore, are conservative risk estimates of potential exposure to dimethoate.

The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios, which cover all the registered uses of dimethoate:

- Mixing/loading liquids and WSPs to support aerial applications,
- Mixing/loading liquids and WSPs to support airblast applications,
- Mixing/loading liquids to support chemigation applications,
- Mixing/loading liquids and WSPs to support groundboom applications,
- Applying sprays with aircraft,
- Applying sprays with groundboom equipment,
- Applying sprays with airblast equipment,
- Flagging to support aerial spray applications,
- Mixing/loading/applying liquids via backpack,
- Mixing/loading/applying liquids via mechanically-pressurized handgun, and
- Mixing/loading/applying liquids via manually-pressurized handwand.

Occupational Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Assumptions and factors, as well as algorithms used to estimate non-cancer exposure and dose for occupational handlers are detailed in the most recent ORE memo (K. Lowe; 15-SEP-2015; D418589).

The steady-state approach is appropriate for dimethoate given the toxicological and exposure profile. The steady-state endpoint selection for dimethoate overlaps with HED's traditional short-term exposure duration endpoint selection and is considered health protective for occupational handlers that apply commercially over longer periods of time (i.e., intermediate-term exposures).

Most of the dimethoate registered labels require handlers to wear a single layer of clothing (long-sleeved shirt and long pants), shoes plus socks, protective eyewear (either goggles or face shield), chemical-resistant gloves, a National Institute for Occupational Safety and Health (NIOSH)-approved dust/mist filtering respirator with Mine Safety and Health Administration (MSHA)/NIOSH approval number prefix TC-21C or a NIOSH-approved respirator with any N, R, P, or HE filter, and a chemical-resistant apron when mixing, loading, cleaning up spills, or equipment.

For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, brain AChE inhibition, is not sex-specific, the female-specific body weight was used to protect for pregnant women due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

Dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were similar. The occupational handler exposure and risk estimates indicate that the dermal and inhalation combined MOEs are of concern to HED (i.e., MOEs ≤ 1000) for most scenarios assuming the use of label-required PPE (noted by the highlighted column in Table 11.1.1 – single layer of clothing, gloves and a PF5 respirator). As was noted above, the inhalation risk estimates are considered to be a conservative estimate of exposure to dimethoate residues considering the inhalation POD was selected from an omethoate toxicity study. Only five scenarios (out of 40) reach an MOE above the LOC of 1000 at some level of PPE (above what is currently required on the labels) or with engineering controls.

HED has no data to assess exposures to pilots using open cockpits. The only data available is for exposure to pilots in enclosed cockpits. Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); per the Agency's Worker Protection Standard stipulations for engineering controls, pilots are not required to wear protective gloves for the duration of the application. With this level of protection, there are no risk estimates of concern for applicators.

The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for human flaggers where appropriate, agricultural aviation has changed dramatically over the past two decades. According the 2012 National Agricultural Aviation Association (NAAA) survey of their membership, the use of Global Positioning System (GPS) for swath guidance in agricultural aviation has grown steadily from the mid-1990s. Over the same time period, the use of human flaggers for aerial pesticide applications has decreased steadily from ~15% in the late 1990s to only 1% in the most recent (2012) NAAA survey. The Agency will continue to monitor all available information sources to best assess and characterize the exposure potential for human flaggers in agricultural aerial applications. **HED recommends that the PPE on the registered dimethoate labels for flaggers be revised to reflect the requirements identified above (and in Table 9.1.1) to reach acceptable MOEs, or that flaggers be prohibited on the label.**

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Dimethoate.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[3]	Area Treated[4]	Total MOE[5] (LOC = 1000)									
						SL/No G No-R	SL/G No-R	DL/G No-R	SL/No G PF5 R	SL/G PF5-R	DL/G PF5-R	SL/No G PF10 R	SL/G PF10-R	DL/G PF10-R	EC
Mixer/Loader															
M/L liquids for aerial applications and chemigation[8]	Nursery	SL/No G 220 SL/G 37.6 DL/G 29.1 EC 8.6	No-R 0.219 PF5 R 0.0438 PF10 R 0.0219 EC 0.083	1 lb ai/A	60 A	**67**	**130**	**140**	**98**	**360**	**420**	**100**	**450**	**540**	**610**
	Orchard[6]			0.33 lb ai/A	350 A	**34**	**70**	**74**	**49**	**190**	**210**	**52**	**240**	**280**	**320**
				1.0 lb ai/A		**11**	**24**	**25**	**16**	**63**	**72**	**17**	**80**	**95**	**110**
				1.33 lb ai/A		**8.6**	**17**	**18**	**12**	**46**	**52**	**13**	**59**	**69**	**78**
	Typical field crops[7]			0.5 lb ai/A		**22**	**46**	**48**	**32**	**120**	**140**	**34**	**150**	**190**	**210**
				1 lb ai/A		**11**	**24**	**25**	**16**	**63**	**72**	**17**	**80**	**95**	**110**
	High-acreage field crops			0.5 lb ai/A	1200 A	**6.7**	**13**	**14**	**9.8**	**36**	**42**	**10**	**45**	**54**	**61**
	Forestry (aerial only)			2 lb ai/A	7500 A	**0.26**	**0.54**	**0.57**	**0.38**	**1.5**	**1.7**	**0.4**	**1.8**	**2.2**	**2.4**
M/L liquids for airblast applications	Nursery			4.15 lb ai/A	20 A	**48**	**100**	**110**	**68**	**260**	**300**	**72**	**330**	**440**	**440**
	Orchard			1.33 lb ai/A	40 A	**74**	**150**	**160**	**110**	**410**	**470**	**110**	**510**	**610**	**690**
M/L liquids for groundboom applications	Nursery			0.5 lb ai/A	60 A	**130**	**270**	**290**	**190**	**700**	**820**	**200**	**890**	1,100	1,200
	Typical field crops			2 lb ai/A	80 A	**25**	**51**	**53**	**36**	**130**	**150**	**38**	**170**	**210**	**230**
	High-acreage field crops			0.5 lb ai/A	200 A	**39**	**79**	**83**	**56**	**220**	**250**	**59**	**270**	**320**	**370**
M/L WSP for aerial applications	Orchard	EC 9.8	EC 0.24	1 lb ai/A	350 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**42**
	High-acreage field crops			0.5 lb ai/A	1,200	ND	ND	ND	ND	ND	ND	ND	ND	ND	**24**
M/L WSP for airblast applications	Orchard			1 lb ai/A	40 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**370**
M/L WSP for groundboom applications	High-acreage field crops			0.5 lb ai/A	200 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**140**

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Dimethoate.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[3]	Area Treated[4]	Total MOE[5] (LOC = 1000)									
						SL/No G No-R	SL/G No-R	DL/G No-R	SL/No G PF5 R	SL/G PF5-R	DL/G PF5-R	SL/No G PF10 R	SL/G PF10-R	DL/G PF10-R	EC
Applicator															
Applying sprays via aerial equipment	Nursery	EC 2.08	EC 0.0049	1 lb ai/A	60 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	2,800
	Orchard			1.33 lb ai/A	350 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**360**
	Typical field crops			1 lb ai/A		ND	ND	ND	ND	ND	ND	ND	ND	ND	**480**
	High-acreage field crops			0.5 lb ai/A	1,200 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**280**
	Forestry			2 lb ai/A	7,500 A	ND	ND	ND	ND	ND	ND	ND	ND	ND	**11**
Applying sprays via airblast equipment[9]	Nursery	SL/No G 1,770 SL/G 1,590 DL/G 1,480 EC 14.6	No-R 4.71 PF5 R 0.942 PF10 R 0.471 EC 0.068	4.15 lb ai/A	20 A	**2.2**	**2.2**	**2.2**	**5.7**	**6.2**	**6.2**	**7.1**	**7.9**	**7.9**	**170**
	Orchard			1.33 lb ai/A	40 A	**3.4**	**3.5**	**3.5**	**8.9**	**9.3**	**9.9**	**11**	**12**	**13**	**260**
Applying sprays via groundboom equipment	Nursery	SL/No G 78.6 SL/G 16.1 DL/G 12.6 EC 5.1	No-R 0.34 PF5 R 0.068 PF10 R 0.034 EC 0.043	0.5 lb ai/A	60 A	**93**	**110**	**110**	**280**	**460**	**470**	**380**	**800**	**850**	2,300
	Typical field crops			2 lb ai/A	80 A	**17**	**19**	**19**	**52**	**84**	**87**	**71**	**150**	**160**	**430**
	High-acreage field crops			0.5 lb ai/A	200 A	**27**	**31**	**31**	**85**	**140**	**140**	**120**	**230**	**250**	**680**
Flagger															
Flagger	Nursery	SL/No G 11 SL/G 12 DL/G 10.6	No-R 0.35 PF5 R 0.07 PF10 R 0.035	1 lb ai/A	60 A	**170**	**170**	**170**	**650**	**630**	**660**	1,000	**950**	1,000	ND
	Orchard			1.33 lb ai/A	350 A	**22**	**22**	**22**	**83**	**81**	**84**	**130**	**120**	**130**	ND
	Typical field crop			1 lb ai/A		**29**	**29**	**30**	**110**	**110**	**110**	**170**	**160**	**170**	ND
	High-acreage field crop			0.5 lb ai/A		**59**	**58**	**59**	**220**	**220**	**220**	**340**	**320**	**350**	ND
Mixer/Loader/Applicator															
M/L/A liquids ground applications (soil directed) with backpack	Orchard	SL/No G 8,260 SL/G 8,260 DL/G 4,120	No-R 2.58 PF5 R 0.516 PF10 R 0.258	0.005 lb ai/gal	40 gal	**710**	**710**	1,200	**820**	**820**	1,600	**830**	**830**	1,600	ND
	Christmas tree farm			0.025 lb ai/gal		**140**	**140**	**250**	**160**	**160**	**320**	**170**	**170**	**330**	ND
	Forestry			0.04 lb ai/gal		**92**	**92**	**150**	**110**	**110**	**200**	**110**	**110**	**200**	ND
	Nursery			0.08 lb ai/gal		**45**	**45**	**79**	**51**	**510**	**100**	**52**	**52**	**110**	ND

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Dimethoate.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[3]	Area Treated[4]	Total MOE[5] (LOC = 1000)									
						SL/No G No-R	SL/G No-R	DL/G No-R	SL/No G PF5 R	SL/G PF5-R	DL/G PF5-R	SL/No G PF10 R	SL/G PF10-R	DL/G PF10-R	EC
M/L/A liquids broadcast applications with backpack	Christmas tree farm	SL/No G 58400 SL/G 30500 DL/G 16900	No-R 69.1 PF5 R 13.8 PF10 R 6.9	0.025 lb ai/gal		**17**	**25**	**34**	**22**	**40**	**64**	**23**	**43**	**72**	ND
	Nursery			0.08 lb ai/gal		**5**	**8**	**11**	**7**	**12**	**20**	**7**	**13**	**23**	ND
	Forestry	SL/No G 8,260 SL/G 8,260 DL/G 4,120	No-R 2.58 PF5 R 0.516 PF10 R 0.258	0.04 lb ai/gal		**11**	**16**	**21**	**14**	**25**	**40**	**14**	**27**	**45**	ND
M/L/A liquids foliar applications with manually-pressurized handgun	Christmas tree farm	SL/No G 100,000 SL/G 430 DL/G 365	No-R 30 PF5 R 6 PF10 R 3	0.025 lb ai/gal	40 gal	**13**	**120**	**130**	**14**	**550**	**560**	**14**	**920**	**970**	ND
	Nursery			0.08 lb ai/gal		**4**	**39**	**40**	**4.3**	**170**	**180**	**4.4**	**290**	**310**	ND
M/L/A liquids foliar applications with mechanically-pressurized handgun	Orchard	SL/No G 6050 SL/G 2050 DL/G 1360	No-R 8.68 PF5 R 1.74 PF10 R 0.87	0.0025 lb ai/gal	1,000 gal	**61**	**110**	**130**	**83**	**210**	**280**	**88**	**230**	**330**	ND
	Christmas tree farm														
	Nursery														
	Typical field crop														
M/L/A liquids drench/soil/ground directed applications with mechanically-pressurized handgun	Orchard														
	Nursery														
	Typical field crop														

Shaded column = current PPE required on labels. Bold MOE values indicate the LOC has been exceeded with label-recommended and/or additional PPE.

1. Typical field crops include asparagus, broccoli, cauliflower, Brussels sprouts, celery, endive, leaf lettuce, Swiss chard, garbanzo beans, kale, lentils, melons, mustard greens, peas, peppers, tomatoes, turnips, and watermelon. High-acreage field crops included alfalfa, beans, corn, cotton, grass grown for seed, potatoes, safflower, sorghum, soybeans, and wheat. Orchard crops include cherries, citrus, pears, and pecans. Nurseries include citrus, lupine, ornamentals in outdoor nurseries. Forestry includes trees grown for pulp.
2. Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (August 2015); Level of mitigation: SL/No G No-R = Single layer clothing, no gloves, no respirator; SL/G No-R = Single layer clothing, gloves, no respirator; DL/G No-R = Double layer clothing, gloves, no respirator; SL/No G PF5 R = Single layer clothing, no gloves, PF5 respirator; SL/G PF5 R = Single layer clothing, gloves, PF5 respirator; DL/G PF5 R = Double layer clothing, gloves, PF5 respirator; SL/No G PF10 R = Single layer clothing, no gloves, PF10 respirator; SL/G PF10 R = Single layer clothing, gloves, PF10 respirator; DL/G PF10 R = Double layer clothing, gloves, PF10 respirator; EC = Engineering Controls. ND = no data.
3. Based on registered labels.
4. Exposure Science Advisory Council Policy #9.1.
5. Total MOE = 1 ÷ (1/Dermal MOE) + (1/Inhalation MOE).
6. Application rates for orchard crops: Pecans (0.33 lb ai/A); Pears and Citrus (1 lb ai/A); Cherries (1.33 lb ai/A).
7. Dimethoate 400 label (67760-118); Label lists maximum application rate for Brussels Sprout as 0.5 lb ai/A, but also indicates 38.2 fl oz. product/A, which is 1 lb ai/A.

8. Only the scenarios assessed at 350 A are applicable for chemigation applications.
9. For airblast applications to nurseries and orchards, additional PPE could include chemical-resistant headgear (CRH). The addition of CRH resulted in MOEs that exceed HED's LOC: Nursery - SL/G/CRH = 24, DL/G/CRH - 27; Orchard SL/G/CRH = 37, DL/G/CRH - 41.

11.2 Short-/Intermediate-Term Post-Application Risk

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

For occupational post-application workers, exposure is anticipated to be to both dimethoate and omethoate. Since the dermal route of exposure is assessed using a dimethoate-specific toxicity study, the omethoate residues have been adjusted by a TAF to account for the increased potency of omethoate.

11.2.1 Occupational Post-application Inhalation Exposure/Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its FIFRA SAP in December 2009, and received the SAP's final report on March 2, 2010[15]. The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis[16]. During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies) or further analysis is required for dimethoate.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the ARTF. Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments.

11.2.2 Occupational Post-application Dermal Exposure/Risk Estimates

Occupational Post-application Dermal Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational post-application risk assessments. Assumptions and factors, as well as the algorithms used to estimate non-cancer exposure and dose for occupational post-application workers are detailed in the most recent ORE memo (K. Lowe; 15-SEP-2015; D418589).

[15] http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html
[16] http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219.

The steady-state approach is appropriate for dimethoate given the toxicological and exposure profile. The "steady-state" endpoint selection for dimethoate overlaps with HED's traditional short-term exposure duration endpoint selection as well as being appropriately health protective for workers that are exposed over longer periods of time (i.e., intermediate-term exposures).

For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, brain AChE inhibition, is not sex-specific, the female-specific body weight was used to protect for pregnant women due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.4).

Chemical-specific DFR data have been submitted for dimethoate. Four studies were submitted that examined residues of dimethoate and its metabolite, omethoate, on the following crops: grapes (MRID 44788201), tomato (MRID 44690302), lettuce (MRID 44690301), and apple (MRID 44827601). All four studies have been reviewed by HED and found to be acceptable for risk assessment. The grape DFR data were not used in this risk assessment since dimethoate is no longer registered for use on grapes.

A summary of how the DFR data were used is summarized in Table 11.2.2.1 and discussed in the most recent ORE memo (K. Lowe; 15-SEP-2015; D418589).

Table 11.2.2.1. Summary of DFR Data Use in Occupational Post-application Assessment for Dimethoate

Crop for which DFR data available	Locations included in study	Crops for which DFR data used as surrogate
Apple	Michigan (MI) - non-arid New York (NY) - non-arid Washington (WA) - arid	Cherries, Christmas trees, Forestry, Grapefruit, Lemons, Ornamentals (nursery crop), Orange, Pear, Pecan
Lettuce	Pennsylvania (PA) - non-arid Florida (FL) - non-arid California (CA) -- arid	Kale, Leaf lettuce, Mustard greens, Green pea, Swiss chard, Turnip
Tomato	Pennsylvania (PA) - non-arid Florida (FL) - non-arid California (CA) -- arid	Alfalfa, Asparagus, Dry beans and peas, Broccoli, Brussels sprouts, Cauliflower, Celery, Field Corn, Pop corn, Cotton, Forage crop, Bell Pepper, Potato, Safflower, Grain sorghum, Soybean, Tomato, Watermelon, Spring wheat, Winter wheat

Each of the studies measured the amount of dimethoate residues remaining on treated leaves following applications, and also measured, when present, omethoate residues. Typically, when omethoate was present in the studies, it peaked in quantity a few days after the application, and then gradually dissipated over time. Dimethoate residues peaked immediately after application and dissipated over time thereafter. In general, omethoate was a significant factor in arid areas (i.e., areas where the average annual rainfall is less than 25 inches per year). Since dissipation rates at the arid sites were significantly different from those at the non-arid sites, the results are reported separately for all study sites.

As mentioned earlier, omethoate is a metabolite of dimethoate and is 3 times more toxicologically potent than dimethoate. Since the POD for the dermal route of exposure was chosen from a dimethoate toxicity study, a TAF of 3 was chosen to account for the increased potency of omethoate in exposure calculations. A total toxic residue approach was used whereby residues of omethoate were adjusted by the TAF and total residues (dimethoate + adjusted omethoate) were included in exposure calculations[17]. In those studies where omethoate was not found, the post-application risks were assessed using only the dimethoate residues.

Occupational Post-application Non-Cancer Dermal Risk Estimates

The post-application exposure scenarios associated with the registered uses of dimethoate are summarized in Tables 11.2.2.2 through 11.2.2.4. The results of the risk assessment for post-application exposures indicate that the location and/or the environmental conditions (i.e., arid versus non-arid) near the time of application influence the length of time following application until risks are below HED's LOC (i.e., MOEs are greater than or equal to 1000) as does the type of plant to which the application is directed. For most crops, the post-application assessment indicates that following applications in arid areas (i.e., outdoor areas where average annual rainfall is less than 25 inches), residues persist longer than in non-arid areas.

For the orchard crops, using the apple DFR data, there are risks of concern for most of the high contact post-application activities associated with each crop (e.g., hand harvesting, handset irrigation, etc). Some crop/activity combinations do not reach an acceptable MOE (LOC = 1000) even up to 30 days after application.

For the field crops using the lettuce DFR data, there are risks of concern for certain high contact activities (e.g., hand harvesting, hand weeding, etc). Some crop/activity combinations do not reach an acceptable MOE (LOC = 1000) until 7 days after application.

For the field crops using the tomato DFR data, there are risks of concern for certain high contact activities (e.g., hand harvesting, hand weeding, etc). Some crop/activity combinations do not reach an acceptable MOE (LOC = 1000) until 14 days after application.

[17] Total DFR, ug/cm^2 = [(Omethoate residue, ug/cm^2) * TAF] + [Dimethoate residue, ug/cm^2)

Table 11.2.2.2. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Apples/MRID 44827601)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
APPLE STUDY DATA																
					MI	NY	WA	MI	NY	WA	MI	NY	WA	MI	NY	WA
Cherry	Tree, "fruit", deciduous	1.33	Orchard maintenance; Weeding, Hand; Bird Control; Propping	100	12 hr			1.89	2.35	2.70	0.022	0.027	0.031	**920**	**740**	**640**
					1	3	6	1.64	1.72	1.63	0.019	0.020	0.019	1,100	1,000	1,100
			Transplanting	230	12 hr			1.89	2.35	2.70	0.050	0.063	0.072	**400**	**320**	**280**
					7	11	15	0.72	0.74	0.76	0.019	0.020	0.020	1,000	1,000	1,000
			Scouting; Pruning, Hand; Training	580	12 hr			1.89	2.35	2.70	0.127	0.158	0.182	**160**	**130**	**110**
					14	20	26	0.28	0.29	0.30	0.019	0.019	0.022	1,100	1,000	1,000
			Harvesting, Hand	1400	12 hr			1.89	2.35	2.70	0.306	0.382	0.439	**66**	**53**	**46**
					20	29	30	0.12	0.11	0.21	0.020	0.018	0.035	1000	1,100	**580**
			Thinning Fruit	3600	12 hr			1.89	2.35	2.70	0.787	0.982	1.128	**26**	**21**	**18**
					27	30	30	0.05	0.10	0.21	0.019	0.042	0.089	1,000	**480**	**230**
Christmas tree	Tree, "fruit", evergreen	1	Weeding, Hand; Grading/Tagging	100	12 hr			1.42	1.77	2.03	0.016	0.021	0.024	1,200	**980**	**860**
					N/A	1	2	N/A	1.59	1.71	N/A	0.018	0.020	N/A	1,100	1,000
			Transplanting	230	12 hr			1.42	1.77	2.03	0.038	0.047	0.054	**530**	**430**	**370**
					5	9	12	0.71	0.69	0.74	0.019	0.018	0.020	1,100	1,100	1,000
			Scouting; Shaping	580	12 hr			1.42	1.77	2.03	0.095	0.119	0.137	**210**	**170**	**150**
					12	17	23	0.27	0.30	0.29	0.018	0.020	0.019	1,100	1,000	1,000
			Harvesting, Hand	1400	12 hr			1.42	1.77	2.03	0.230	0.287	0.330	**88**	**70**	**61**
					18	26	30	0.12	0.12	0.16	0.020	0.019	0.026	1,000	1,100	**780**
			Irrigation (hand set)	1900	12 hr			1.42	1.77	2.03	0.312	0.390	0.447	**65**	**52**	**45**
					20	29	30	0.09	0.08	0.16	0.020	0.019	0.035	1,000	1,100	**570**
Forestry	Unassigned	2	Weeding, Hand	100	12 hr			2.84	3.54	4.06	0.033	0.041	0.047	**610**	**490**	**430**
					4	7	10	1.64	1.70	1.74	0.019	0.020	0.020	1,100	1,000	1,000

Table 11.2.2.2. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Apples/MRID 44827601)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
APPLE STUDY DATA																
					MI	NY	WA	MI	NY	WA	MI	NY	WA	MI	NY	WA
			Transplanting	230	12 hr			2.84	3.54	4.06	0.076	0.094	0.108	**270**	**210**	**190**
					10	15	20	0.72	0.74	0.75	0.019	0.020	0.020	1,100	1,000	1,000
			Pruning, Hand	580	12 hr			2.84	3.54	4.06	0.191	0.238	0.273	**110**	**85**	**74**
					17	24	30	0.28	0.29	0.32	0.019	0.019	0.018	1,100	1,000	**940**
			Harvesting, Seed Cone (Conifers)	1400	12 hr			2.84	3.54	4.06	0.460	0.574	0.659	**44**	**35**	**31**
					23	30	30	0.12	0.15	0.32	0.020	0.025	0.044	1,000	**810**	**390**
			Irrigation (hand set)	1900	12 hr			2.84	3.54	4.06	0.625	0.779	0.895	**32**	**26**	**23**
					25	30	30	0.09	0.15	0.32	0.020	0.034	0.060	1,000	**600**	**290**
			Harvesting, Seedling Production	6700	12 hr			2.84	3.54	4.06	2.203	2.749	3.156	**9.2**	**7.3**	**6.4**
					30	30	30	0.05	0.15	0.32	0.036	0.119	0.210	**560**	**170**	**81**
Grapefruit, Lemon, Orange	Tree, "fruit", evergreen	1	Orchard maintenance; Weeding, Hand; Baiting/Trapping; Weeding, Hand	100	12 hr			1.42	1.77	2.03	0.016	0.08	0.024	1,200	**980**	**860**
					N/A	1	2	N/A	1.59	1.71	N/A	0.018	0.020	N/A	1,100	1,000
			Transplanting	230	12 hr			1.42	1.77	2.03	0.038	0.047	0.054	**530**	**430**	**370**
					5	9	12	0.71	0.69	0.74	0.019	0.018	0.020	1,100	1,100	1,000
			Scouting; Pruning, Hand	580	12 hr			1.42	1.77	2.03	0.095	0.119	0.137	**210**	**170**	**150**
					12	17	23	0.27	0.30	0.29	0.018	0.020	0.019	1,100	1,000	1,000
			Harvesting, Hand	1400	12 hr			1.42	1.77	2.03	0.230	0.287	0.330	**88**	**70**	**61**
					18	26	30	0.12	0.12	0.16	0.020	0.019	0.26	1,000	1,100	**780**
Nursery Crop (Ornamentals, Non-bearing Plants)	Unassigned	4.15	Harvesting, Hand; Pruning, Hand; Scouting; Container Moving; Weeding, Hand; Transplanting; Grafting; Propagating;	230	12 hr			5.89	7.34	8.43	0.157	0.196	0.225	**130**	**100**	**90**
					15	22	29	0.75	0.73	0.72	0.020	0.020	0.019	1,000	1,000	1,000

Table 11.2.2.2. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Apples/MRID 44827601)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
APPLE STUDY DATA																
					MI	NY	WA	MI	NY	WA	MI	NY	WA	MI	NY	WA
			Pinching; Tying/Training													
			Irrigation (hand set)	1900	12 hr			5.89	7.34	8.43	1.296	1.617	1.857	**16**	**12**	**11**
					30	30	30	0.10	0.32	0.67	0.021	0.070	0.147	**950**	**290**	**140**
		1	Harvesting, Hand; Pruning, Hand; Scouting; Container Moving; Weeding, Hand; Transplanting; Grafting; Propagating; Pinching; Tying/Training	230	12 hr			1.42	1.77	2.03	0.038	0.047	0.054	**530**	**430**	**370**
					5	9	12	0.71	0.69	0.74	0.019	0.018	0.020	1,100	1,100	1,000
			Irrigation (hand set)	1900	12 hr			1.42	1.77	2.03	0.312	0.316	0.447	**65**	**52**	**45**
					20	29	30	0.03	0.08	0.14	0.020	0.019	0.035	1,000	1,100	**570**
Pear	Tree, "fruit", deciduous	1	Orchard maintenance; Weeding, Hand; Propping	100	12 hr			1.42	1.77	2.03	0.016	0.021	0.024	1,200	**980**	**860**
					N/A	1	2	N/A	1.59	1.71	N/A	0.018	0.020	N/A	1,100	1,000
			Transplanting	230	12 hr			1.42	1.77	2.03	0.038	0.042	0.054	**530**	**430**	**370**
					5	9	12	0.71	0.69	0.74	0.019	0.018	0.020	1,100	1,100	1,000
			Scouting; Pruning, Hand; Training	580	12 hr			1.42	1.77	2.03	0.095	0.107	0.137	**210**	**170**	**150**
					12	17	23	0.27	0.30	0.29	0.018	0.020	0.019	1,100	1,000	1,000
			Harvesting, Hand	1400	12 hr			1.42	1.77	2.03	0.230	0.287	0.330	**88**	**70**	**61**
					18	26	30	0.12	0.12	0.16	0.020	0.019	0.026	1,000	1,100	**780**
			Thinning Fruit	3600	12 hr			1.42	1.77	2.03	0.592	0.738	0.848	**34**	**27**	**24**
					25	30	30	0.05	0.08	0.16	0.019	0.032	0.067	1,100	**630**	**300**
Pecan	Tree, "nut"	0.33	Poling; Orchard maintenance; Weeding, Hand	100	12 hr			0.47	0.58	0.67	0.005	0.007	0.008	3,700	3,000	2,600

Table 11.2.2.2. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Apples/MRID 44827601)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)		DFR[1]		Dermal Dose (mg/kg/day)[2]		MOE[3] (LOC = 1000)	
					Non-Arid	Arid	Non-Arid	Arid	Non-Arid	Arid	Non-Arid	Arid
APPLE STUDY DATA												
					MI	**NY**	**WA**	**MI**	**NY**	**WA**	**MI**	**NY**	**WA**	**MI**	**NY**	**WA**	**MI**	**NY**	**WA**
			Harvesting, Mechanical (shaking)	190							0.010	0.013	0.015	2,000	1,600	1,400
			Transplanting	230							0.012	0.016	0.018	1,600	1,300	1,100
			Pruning, Hand; Scouting	580							0.031	0.039	0.045	640	**510**	**450**
					4	7	10	0.27	0.28	0.29	0.018	0.019	0.019	1,100	1,100	1,000

Bold MOE values are below the LOC of 1000. Shaded cells indicate the MOE is still below the LOC 30 days after application (i.e., an REI of >30 days would be necessary to achieve a MOE greater than the LOC).

1. DFR = Combined residues of dimethoate and omethoate from an apple study, adjusted to account for application rate differences and for differences in toxicity of omethoate.
2. Daily Dermal Dose = [DFR (µg/cm^2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ÷ BW (69 kg).
3. MOE = POD (20.2 mg/kg/day) / Daily Dermal Dose.

Table 11.2.2.3. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Lettuce/MRID 44690301)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)		DFR[1]		Dermal Dose (mg/kg/day)[2]		MOE[3] (LOC = 1000)	
					Non-Arid	Arid	Non-Arid	Arid	Non-Arid	Arid	Non-Arid	Arid
LETTUCE STUDY DATA												
					PA	**FL**	**CA**	**PA**	**FL**	**CA**	**PA**	**FL**	**CA**	**PA**	**FL**	**CA**	**PA**	**FL**	**CA**
Kale, Leaf Lettuce, Mustard Green, Swiss Chard	Vegetable, leafy	0.25	Weeding, Hand; Thinning Plants	70	12 hr			0.27	0.11	0.52	0.002	0.001	0.004	9,100	24,000	4,800
			Scouting	210							0.007	0.003	0.013	3,000	7,800	1,600
			Transplanting	230							0.007	0.003	0.014	2,800	7,200	1,500
			Harvesting, Hand	1100							0.035	0.014	0.066	**580**	1,500	**310**
					1	N/A	5	0.10	N/A	0.15	0.012	N/A	0.019	1,700	N/A	1,100
			Irrigation (hand set)	1900	12 hr			0.27	0.11	0.52	0.060	0.023	0.114	**340**	**870**	**180**
					2	1	7	0.03	0.04	0.09	0.007	0.009	0.020	2,800	2,300	1,000
		0.16	Weeding, Hand	70	12 hr			0.17	0.07	0.33	0.001	0.001	0.003	14,000	37,000	7,500

Table 11.2.2.3. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Lettuce/MRID 44690301)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
LETTUCE STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
Pea, Green	Field / row crop, low / medium		Scouting	210							0.004	0.002	0.008	4,700	12,000	2,500
			Harvesting, Hand	1100							0.022	0.009	0.042	**910**	2,300	**480**
					1	N/A	3	0.06	N/A	0.16	0.008	N/A	0.020	2,600	N/A	1,000
			Irrigation (hand set)	1900	12 hr			0.17	0.07	0.33	0.039	0.015	0.073	**520**	1,400	**280**
					1	N/A	6	0.06	N/A	0.08	0.013	N/A	0.017	1,500	N/A	1,200
Turnip	Vegetable, "root"	0.25	Weeding, Hand; Thinning Plants	70	12 hr			0.27	0.11	0.52	0.002	0.001	0.004	9,100	24,000	4,800
			Scouting	210							0.007	0.003	0.013	3,000	7,800	1,600
			Harvesting, Hand	1100							0.035	0.014	0.066	**580**	1,500	**310**
					1	N/A	5	0.10	N/A	0.15	0.012	N/A	0.019	1,700	N/A	1,100
			Irrigation (hand set)	1900	12 hr			0.27	0.11	0.52	0.060	0.023	0.114	**340**	**870**	**180**
					2	1	7	0.03	0.04	0.09	0.007	0.009	0.020	2,800	2,300	1,000

Bold MOE values are below the LOC of 1000.

1. DFR = Combined residues of dimethoate and omethoate from a lettuce study, adjusted to account for application rate differences and for differences in toxicity of omethoate.
2. Daily Dermal Dose = [DFR ($\mu g/cm^2$) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ÷ BW (69 kg).
3. MOE = POD (20.2 mg/kg/day) / Daily Dermal Dose.

Table 11.2.2.4. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Tomato/MRID 44690302)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
TOMATO STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
		0.5	Scouting	1100	12 hr			0.48	0.66	0.36	0.061	0.084	0.046	**330**	**240**	**440**

Table 11.2.2.4. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Tomato/MRID 44690302)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
TOMATO STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
Alfalfa, Dry Beans, Dry Peas, Forage Crop	Field / row crop, low / medium				2	2	4	0.06	0.11	0.16	0.008	0.006	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Asparagus	Vegetable, stem / stalk	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
			Transplanting	230							0.013	0.018	0.010	1,600	1,100	2,100
			Harvesting, Hand	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Broccoli, Cauliflower	Vegetable, head and stem Brassica	0.5	Transplanting	230	12 hr			0.48	0.66	0.36	0.013	0.018	0.010	1,600	1,100	2,100
			Scouting Thinning Plants	330							0.018	0.025	0.014	1,100	**800**	1,500
					N/A	1	N/A	N/A	0.27	N/A	N/A	0.010	N/A	N/A	2,000	N/A
			Weeding, Hand	1400	12 hr			0.48	0.66	0.36	0.077	0.107	0.058	**260**	**190**	**350**
					2	2	6	0.06	0.11	0.10	0.010	0.017	0.017	2,000	1,200	1,200
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
			Scouting Harvesting, Hand Weeding, Hand	4200	12 hr			0.48	0.66	0.36	0.232	0.322	0.174	**87**	**63**	**120**
					3	4	11	0.02	0.02	0.04	0.011	0.009	0.018	1,800	2,400	1,100
Brussels Sprouts	Vegetable, head and stem Brassica	1	Transplanting	230	12 hr			0.95	1.32	0.71	0.025	0.035	0.019	**800**	**570**	1,100
					1	1	N/A	0.35	0.53	N/A	0.009	0.014	N/A	2,200	1,400	N/A
			Scouting	330	12 hr			0.95	1.32	0.71	0.036	0.051	0.027	**560**	**400**	**740**

Table 11.2.2.4. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Tomato/MRID 44690302)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
TOMATO STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
					1	2	2	0.35	0.21	0.58	0.013	0.008	0.018	1,500	2,500	1,100
			Irrigation (hand set)	1900	12 hr			0.95	1.32	0.71	0.210	0.291	0.157	**96**	**69**	**130**
					3	3	10	0.05	0.09	0.09	0.010	0.019	0.020	2,000	1,100	1,000
			Scouting Harvesting, Hand Topping Weeding, Hand	4200	12 hr			0.95	1.32	0.71	0.463	0.644	0.348	**44**	**31**	**58**
					4	4	14	0.02	0.03	0.04	0.008	0.017	0.020	2,500	1,200	1,000
Celery	Vegetable, leafy	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
			Transplanting	230							0.013	0.018	0.010	1,600	1,100	2,100
			Harvesting, Hand	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Field Corn and Popcorn	Field / row crop, tall	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
				1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.016	0.008	0.014	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Cotton	Field / row crop, low / medium	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
Pepper, bell	Vegetable, fruiting	0.33	Weeding, Hand	70				0.31	0.44	0.24	0.003	0.004	0.002	7,900	5,700	11,000

Table 11.2.2.4. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Tomato/MRID 44690302)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
TOMATO STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
			Scouting	210							0.008	0.011	0.006	2,600	1,900	3,500
			Transplanting	230							0.008	0.012	0.006	2,400	1,700	3,200
			Harvesting, Hand Tying/Training	1100							0.040	0.056	0.030	**500**	**360**	**670**
					1	2	2	0.17	0.07	0.16	0.015	0.009	0.020	1,400	2,200	1,000
			Irrigation (hand set)	1900	12 hr			0.31	0.44	0.24	0.069	0.096	0.052	**290**	**210**	**390**
					2	2	5	0.06	0.07	0.08	0.009	0.016	0.019	2,200	1,300	1,100
Potato	Vegetable, "root"	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
			Irrigation (hand set)	1900							0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Safflower	Field / row crop, low / medium	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,000
Sorghum, grain	Field / row crop, tall	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300
Soybean	Field / row crop, low / medium	0.5	Weeding, Hand	70							0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,000
Tomato	Vegetable, fruiting	0.5	Pruning, Hand Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	210							0.012	0.016	0.009	1,700	1,300	2,300

Table 11.2.2.4. Dimethoate Occupational Post-application Risk Estimates Using Chemical-specific Data (Tomato/MRID 44690302)

Crop	Policy Crop Group Category	Application Rate (lb ai/A)	Activities	Transfer Coefficients (cm^2/hr)	Time Following Application (days, unless specified)			DFR[1]			Dermal Dose (mg/kg/day)[2]			MOE[3] (LOC = 1000)		
					Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid	Non-Arid		Arid
TOMATO STUDY DATA																
					PA	FL	CA	PA	FL	CA	PA	FL	CA	PA	FL	CA
			Transplanting	230							0.013	0.018	0.010	1,600	1,100	2,100
			Harvesting, Hand Tying/Training	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,000
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Watermelon	Vegetable, cucurbit	0.5	Scouting Weeding, Hand Pruning, Hand Thinning Fruit	90	12 hr			0.48	0.66	0.36	0.005	0.007	0.004	4,100	2,900	5,400
			Transplanting	230							0.013	0.018	0.010	1,600	1,100	2,100
			Harvesting, Hand Turning Harvesting, Mechanically-assisted Training	550							0.030	0.042	0.023	**670**	**480**	**890**
					2	1	1	0.06	0.27	0.29	0.011	0.017	0.019	1,800	1,200	1,100
			Irrigation (hand set)	1900	12 hr			0.48	0.66	0.36	0.105	0.146	0.079	**190**	**140**	**260**
					2	3	7	0.06	0.04	0.09	0.014	0.010	0.019	1,400	2,100	1,100
Wheat (spring and winter)	Field / row crop, low / medium	0.5	Weeding, Hand	70	12 hr			0.48	0.66	0.36	0.004	0.005	0.003	5,200	3,800	7,000
			Scouting	1100							0.061	0.084	0.046	**330**	**240**	**440**
					2	2	4	0.06	0.11	0.16	0.008	0.014	0.020	2,500	1,500	1,100

Bold MOE values are below the LOC of 1000.

1. DFR = Combined residues of dimethoate and omethoate from a tomato study, adjusted to account for application rate differences and for differences in toxicity of omethoate.
2. Daily Dermal Dose = [DFR ($\mu g/cm^2$) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ÷ BW (69 kg).
3. MOE = POD (20.2 mg/kg/day) / Daily Dermal Dose.

Restricted-Entry Interval (REI)

Current product-label REIs range from 48 hours to 24 days depending on the crop and location (i.e., arid versus non-arid areas). Based on the current post-application dermal exposure assessment (Tables 11.2.2.2 - 11.2.2.4), REIs of 12 hours to more than 30 days would be necessary to reach acceptable MOEs (i.e., MOEs ≥ 1000) from exposure to the combined residues of dimethoate and omethoate. Table 11.2.2.5 provides a summary of the current REIs on product labels and the REIs based on the quantitative post-application exposure assessment for dimethoate that would be needed to achieve risks that were not of concern.

Even though REIs of 12 and 24 hours are long enough for MOEs to reach the LOC of 1000 for some crops/activities, HED recommends a minimum REI of 48 hours (72 hours in arid regions) to be protective of potential for exposure to omethoate, which is known to form after application. These REIs are in line with the 40 CFR 156.208 (c) (2) assignments for active ingredients that are classified as Toxicity Category I for acute dermal, eye irritation, and primary skin irritation.

Table 11.2.2.5. Summary of Restricted Entry Intervals

Crop		Current REI on product labels		HED recommended REI	
		Non-Arid	Arid	Non-Arid	Arid
Cherry		10 days	14 days	>30 days	>30 days
Christmas tree		10 days	14 days	29 days	>30 days
Forestry		14 days	24 days	>30 days	>30 days
Grapefruit		10 days	14 days	26 days	>30 days
Lemon		10 days	14 days	26 days	>30 days
Orange		10 days	14 days	26 days	>30 days
Nursery Crop (Ornamentals, Non-bearing Plants)	Woody ornamentals	10 days	14 days	29 days (>30 days if airblast >1 lb ai/A)	>30 days (>30 days if airblast >1 lb ai/A)
	Herbaceous ornamentals	48 hours			
	Conifer seed orchards	48 hours (16 days if airblast >1 lb ai/A)	4 days (25 days if airblast >1 lb ai/A)		
Pear		10 days	14 days	>30 days	>30 days
Pecan		48 hours		7 days	10 days
Kale				48 hours[1]	7 days
Lettuce, leaf					
Mustard Green					
Swiss Chard					
Pea, Green				48 hours[1]	6 days
Turnip				48 hours[1]	7 days
Alfalfa				3 days	7 days
Asparagus					
Bean, dry, and Pea, dry					
Broccoli		48 hours	72 hours	4 days	11 days
Brussels Sprouts		48 hours	72 hours	4 days	14 days
Cauliflower		48 hours	72 hours	4 days	11 days
Celery		48 hours		3 days	7 days
Field Corn and Popcorn		48 hours (4 days for detasseling)	48 hours (15 days for detasseling)	3 days	7 days
Cotton		48 hours		48 hours[1]	72 hours[1]

Table 11.2.2.5. Summary of Restricted Entry Intervals				
Crop	Current REI on product labels		HED recommended REI	
	Non-Arid	Arid	Non-Arid	Arid
Forage Crop	48 hours		3 days	7 days
Pepper, bell	48 hours		2 days	5 days
Potato	48 hours		3 days	7 days
Safflower	48 hours		3 days	7 days
Sorghum, grain	48 hours		48 hours[1]	72 hours[1]
Soybean	48 hours		48 hours	4 days
Tomato	48 hours		3 days	7 days
Watermelon	48 hours		3 days	7 days
Wheat (spring and winter)	48 hours		48 hours	4 days

1. Even though REIs of 12 and 24 hours are long enough for MOEs to reach the LOC of 100 for some crops/activities, HED recommends a minimum REI of 48 hours (72 hours in arid regions) for the product labels to be protective of the acute toxicity of omethoate.

12.0 References

Dimethoate. Response to Waiver Request on Residue Data Requirements. D357808, 07-JAN-2010, M. Sahafeyan.

Dimethoate. Response to Reregistration Requirements: Supplemental Data Pertaining to Characterization of Radioactive Residues in Milk, Radiovalidation of the Livestock Analytical Method, Storage Stability Intervals, Magnitude of Residues for Cotton Gin By-Product and Alfalfa Grown for Seed, Safflower Processing and an (Unsolicited) Olive Metabolism Study. D232849, 24-MAY-2011, M. Sahafeyan.

Dimethoate. Response to Deficiency: New Ruminant and Poultry Livestock Feeding Studies; A New Enforcement Method for Livestock Commodities Including a Final Method Validation; Storage Stability of Livestock Tissues; Magnitude of Residues on Grass Grown for Seed. D239886, 12-NOV-2013, M. Sahafeyan.

Tier II Drinking Water Assessment for Dimethoate for the Use in Human Health Risk Assessment in the Registration Review Risk Assessment. D415002, 28-JUL-2014, J. Meléndez.

Bouchard MF, Chevrier J, Harley KG, Kogut K, Vedar M, Calderon N, et al. Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year-Old Children. Environ Health Perspectives. 2011;119:1189-1195.

Bouchard M.F., Bellinger D.C., Wright R.O., Weisskopf M.G., (2010). Attention-Deficit/Hyperactivity Disorder and Urinary Metabolites of Organophosphate Pesticides. PEDIATRICS DOI:10.1542/peds.2009-3058.

Chen L, Zhao T, Pan C, Ross JH, Krieger RI. (2012) Preformed biomarkers including dialkylphosphates (DAPs) in produce may confound biomonitoring in pesticide exposure and risk assessment. J Agric Food Chem. 2012 Sep 12;60(36):9342-51. doi: 10.1021/jf303116p. Epub 2012 Sep 4.

Engel SM, Berkowitz GS, Barr DB, Teitelbaum SL, Siskind J, Meisel SJ, Wetmur JG, Wolff MS. Prenatal Organophosphate Metabolite and Organochlorine Levels and Performance on the Brazelton Neonatal Behavioral Assessment Scale in a Multiethnic Pregnancy Cohort. American Journal of Epidemiology. 2007;165:1397-1404.

Engel SM, Wetmur J, Chen J, Zhu C, Barr DB, Canfield RL, Wolff MS. Prenatal Exposure to Organophosphates, Paraoxonase 1, and Cognitive Development in Childhood. Environmental Health Perspectives. 2011;119:1182-1188.

Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of in Utero Organophosphate Pesticide Exposure and Fetal Growth and Length of Gestation in an Agricultural Population. Environmental Health Perspectives. 2004;115:792–798.

Eskenazi B, Marks AR, Bradman A, Harley K, Barr DB, Johnson C, Morga N, Jewell NP. Organophosphate Pesticide Exposure and Neurodevelopment in Young Mexican-American Children. Environmental Health Perspectives. 2007;115:792–798.

FIFRA Scientific Advisory Panel. (2012). Transmittal of the Meeting Minutes from the FIFRA Scientific Advisory Panel Meeting of April 10-12, 2012. FIFRA Scientific Advisory Panel, Office of Science Coordination and Policy, Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency. Washington, DC. Available: http://www.epa.gov/scipoly/sap/meetings/2012/041012meeting.html

Fortenberry, GZ, Meeker, JD, Sánchez, BN, Barr, DB, Panuwet, P, Bellinger, D, Schnaas, L, Solano-González, M, Ettingera, AS, Hernandez-Avila, M, Hu, H, Tellez-Rojoj, MM. Urinary 3,5,6-trichloro-2-pyridinol (TCPY) in pregnant women from Mexico City: Distribution, temporal variability, and relationship with child attention and hyperactivity. International Journal of Hygiene and Environmental Health 217 (2014): 405–412.

Forsberg ND, Rodriguez-Proteau R, Mab L, Morréc J, Christensen JM, Maierc CS, Jenkins JJ, Anderson KA. Organophosphorus pesticide degradation product in vitro metabolic stability and time-course uptake and elimination in rats following oral and intravenous dosing. Xenobiotica, 2011; 41(5): 422–429.

Furlong, Melissa A., Engel, Stephanie M., Boyd Barr, Dana, Wolff, Mary S. Prenatal exposure to organophosphate pesticides and reciprocal social behavior in childhood. 2014. Environment International 70:125-131.

Guodong, Ding, Pei, Wang, Ying, Tian, Jun, Zhang, Yu, Gao, Xiaojin, Wang, Rong, Shi, Guoquan, Wang, and Xiaoming, Shen. Organophosphate Pesticide Exposure and Neurodevelopment in Young Shanghai Children. Environmental Science and Technology 46:2911-2917, 2012.

Marks AR, Harley K, Bradman A, Kogut K, Barr DB, Johnson C, et al. Organophosphate Pesticide Exposure and Attention in Young Mexican-American Children: The CHAMACOS Study. Environmental Health Perspectives. 2010;118:1768-1774.

Oulhote, Youssef and Bouchard, Maryse F. Urinary Metabolites of Organophosphate and Pyrethroid Pesticides and Behavioral Problems in Canadian Children. Environmental Health Perspectives. 121:1378-1384 (2013)

Racke J.D. Degradation of organophosphorous insecticidesin environmental matrices. In: Organophosphates Chemistry, Fate and Effects. Academic Press, Inc., San Diego, CA, 1992, pp 47–72.

Rauh VA, Garfinkel R, Perera FP, Andrews HF, Hoepner L, Barr DB, Whitehead R, Tang D, Whyatt RW. Impact of Prenatal Chlorpyrifos Exposure on Neurodevelopment in the First 3 Years of Life Among Inner-City Children. Pediatrics. 2006;18(6): 1835-1859.

Rauh V, Arunajadai S, Horton M, Perera F, Hoepner L, Barr DB, et al. 2011. Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide. Environmental Health Perspectives. 2011;119:1196-1201.

Shelton, Janie F., Geraghty, Estella M., Tancredi, Daniel J., Delwiche, Lora D., Schmidt, Rebecca J., Ritz, Beate, Hansen, Robin L., and Hertz-Picciotto, Irva. Neurodevelopmental disorders and prenatal residential proximity to agricultural pesticides: The CHARGE Study. Environmental Health Perspectives 122:1103–1109, 2014.

U.S. Environmental Protection Agency. (2008). Draft Science Issue Paper: Chlorpyrifos Hazard and Dose Response Characterization. http://www.epa.gov/scipoly/sap/meetings/2008/091608_mtg.htm

U.S. Environmental Protection Agency. (2012). Draft Issue Paper: Scientific Issues Concerning Health Effects of Chlorpyrifos. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0040-0002

Young JG, Eskenazi B, Gladstone EA, Bradman A, Pedersen L, Johnson C, Barr DB, Furlong CE, Holland NT. Association Between In Utero Organophosphate Pesticide Exposure and Abnormal Reflexes in Neonates. NeuroToxicology. 2005;26:199–209.

Zhang, Ying, Han, Song, Liang, Duohong, Shi, Xinzhu, Wang, Fengzhi, Wei Liu, Zhang, Li, Chen, Lixin, Gu, Yingzi, Tian, Ying. Prenatal exposure to organophosphate pesticides and neurobehavioral development of neonates: A birth cohort study in Shenyang, China. PlosOne 47:80–85, 2014.

Zhang X, Driver JH, Li Y, Ross JH, Krieger RI. (2008) Dialkylphosphates (DAPs) in fruits and vegetables may confound biomonitoring in organophosphorus insecticide exposure and risk assessment. J Agric Food Chem. 2008 Nov 26;56(22):10638-45. doi: 10.1021/jf8018084.

RDI: RAB1 (9/15/2015)
cc: M.M. Perron
M.M. Perron: S10955:PY-S:(703)347-0395:7509P:RAB1

Appendix A. Toxicology Profile

A.1 Toxicology Data Requirements

Study requirements (40 CFR 158.340) for dimethoate are presented below. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Acute Eye Irritation	yes	yes
870.2500	Acute Dermal Irritation	yes	yes
870.2600	Skin Sensitization	yes	yes
870.3100	90-Day Oral Toxicity in Rodents	yes	yes
870.3150	90-Day Oral Toxicity in Nonrodents	yes	yes
870.3200	21/28-Day Dermal Toxicity	yes	yes
870.3250	90-Day Dermal Toxicity	no	--
870.3465	90-Day Inhalation Toxicity	yes	yes[1]
870.3700a	Prenatal Developmental Toxicity (rodent)	yes	yes
870.3700b	Prenatal Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction and Fertility Effects	yes	yes
870.4100a	Chronic Toxicity (rodent)	yes	yes[2]
870.4100b	Chronic Toxicity (nonrodent)	yes	yes
870.4200a	Carcinogenicity (rat)	yes	yes[2]
870.4200b	Carcinogenicity (mouse)	yes	yes
870.4300	Combined Chronic Toxicity/Carcinogenicity	yes	yes
870.5100	Mutagenicity—Bacterial Reverse Mutation Test	yes	yes
870.5300	Mutagenicity—Mammalian Cell Gene Mutation Test	yes	yes
870.5xxx	Mutagenicity— Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100	Acute Delayed Neurotoxicity (hen)	no	--
870.6200a	Acute Neurotoxicity Screening Battery (rat)	yes	yes
870.6200b	90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300	Developmental Neurotoxicity	yes	yes
870.7485	Metabolism and Pharmacokinetics	yes	yes
870.7600	Dermal Penetration	no	--
870.7800	Immunotoxicity	yes	yes

[1] An inhalation study with omethoate, which is more potent than dimethoate, is available.
[2] The combined chronic toxicity/carcinogenicity study satisfies the requirement of the study.

A.2. Toxicity Profiles

Table A.2.1. Acute Toxicity Profile - Dimethoate				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral (rat)	48890603	LD50 = 550 mg/kg (F)	III
870.1200	Acute dermal (rabbit)	48890604	LD50 > 5000 mg/kg	IV
870.1300	Acute inhalation (rat)	48890605	LC50 > 2.1 mg/L	IV
870.2400	Acute eye irritation (rabbit)	48890606	Moderate irritant	II
870.2500	Acute dermal irritation (rabbit)	48890607	Not a dermal irritant	IV
870.2600	Skin sensitization (guinea pig)	48890608	Not a sensitizer	N/A

Table A.2.2. Acute Toxicity Profile - Omethoate				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral (rat)	46099809	LD50= 22/28 mg/kg (M/F)	I
870.1200	Acute dermal (rat)	46099810	LD50= 215 mg/kg	I
870.1300	Acute inhalation (rat)	46099813	LC50= 0.28 mg/kg	II

Note: Studies have not been updated to reflect current HED policy. Endpoint selection was driven by BMD modeling of the AChE activity to obtain BMD_{10} and $BMDL_{10}$ values. As a result, updates to NOAEL/LOAEL values (or NOEL/LOEL values) in these studies would not ultimately impact current PODs or risk estimates. Consequently, the Agency did not find it necessary to update these studies at this time.

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100	90-Day Oral Toxicity in Rodents (rat)	00051675, 0077532 0,2,8,32,50, or 400 ppm (0, 0.1, 0.4, 1.6, 2.5, or 20 mg/kg/d) Acceptable/guideline	Cholinesterase NOEL = 32 ppm (1.6 mg/kg/d) Cholinesterase LOEL = 50 ppm (2.5 mg/kg/d) based on the depression of plasma, RBC, and brain cholinesterase Systemic NOEL = 50 ppm (2.5 mg/kg/d) Systemic LOEL = 400 ppm (20 mg/kg/d) based on decreased growth and food consumption and increased kidney and liver weight ratios
870.3150	90-Day Oral Toxicity in Non-Rodent (dog)	00051676 0, 2, 10, 50, or 1500-3000 ppm (0, 0.05, 0.25, 1.25, or 37.5-75 mg/kg/d) Acceptable/Non-guideline (with chronic dog)	Cholinesterase NOEL = 2 ppm (0.05 mg/kg/d) Cholinesterase LOEL = 10 ppm (0.25 mg/kg/d) based on depression of RBC cholinesterase Systemic NOEL = 50 ppm (1.25 mg/kg/d) Systemic LOEL = 1500 ppm (37.5 mg/kg/d) based on tremors and decreased food consumption in females Only 1-2 dogs treated per group

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3200	Dermal Toxicity (rat) 5-day exposure (using 43.5% a.i. formulation)	44818902 (1999) 0, 5, 10, 20, 40, or 100 mg/kg/d Acceptable/non-guideline	Males: NOAEL = 40 mg/kg/d LOAEL = 100 mg/kg/d based on statistically significant inhibition of RBC and brain cholinesterase activity Females: NOAEL = 10 mg/kg/d LOAEL = 20 mg/kg/d based on statistically significant inhibition of RBC and brain cholinesterase activity
870.3200	28-Day Dermal Toxicity (rat)	44999101 (1999) 0, 10.5, 21, 31.5, or 63 mg/kg/d Acceptable/guideline	NOAEL = 10.5 mg/kg/d LOAEL = 21 mg/kg/d based on reduced brain cholinesterase activity (both sexes) No systemic or dermal toxicity
870.3700a	Prenatal Developmental in Rodent (rat)	00150130 (1984) 0, 3, 6, or 18 mg/kg/d Acceptable/guideline	Maternal NOEL = 3 mg/kg/d Maternal LEL = 6 mg/kg/d based on increased reaction to sounds and touch stimuli, body tremors, and unsteady gate Developmental NOEL = 18 mg/kg/d Developmental LEL not established
870.3700b	Prenatal Developmental in Non-Rodent (rabbit)	00149126, 00159760 (1984) 0, 10, 20 or 40 mg/kg/d Acceptable/guideline	Maternal NOEL = 10 mg/kg/d Maternal LEL = 20 mg/kg/d based on decreased food consumption and clinical signs Developmental NOEL = 20 mg/kg/d Developmental LEL = 40 mg/kg/d based on decreased fetal body weight
870.3800	Reproduction and Fertility Effects (rat)	42251501 (1992) 0, 1, 15, or 65 ppm (0, 0.08, 1.2, or 5.46 mg/kg/d) Acceptable/guideline	Cholinesterase NOEL = 0.08 mg/kg/d Cholinesterase LEL = 1.2 mg/kg/d based on decreased plasma, erythrocyte and brain cholinesterase activity Parental NOEL = 0.08 mg/kg/d Parental LEL = 1.2 mg/kg/d based on decreased cholinesterase activity in both sexes and generations Reproductive NOEL = 1.2 mg/kg/d Reproductive LEL= 5.46 mg/kg/d based on decreased fertility index, pup survival and body weights

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800	Reproduction and Fertility Effects (rat)	46181001 (2003) 0, 0.2, 1, or 6.5 mg/kg/d Acceptable/guideline	Parental NOAEL = 0.2 mg/kg/d Parental LOAEL = 1 mg/kg/d based on decreased erythrocyte and brain cholinesterase activity Offspring NOAEL = 1 mg/kg/d Offspring LOAEL = 6.5 mg/kg/d based on decreased brain cholinesterase activity in females Developmental NOAEL = 6.5 mg/kg/d Developmental LOAEL = not established
870.3800	Reproduction and Fertility Effects (rat) One-generation range finding	46348201 (1990) 0, 50, 75, or 100 ppm (0, 2.9, 4.4, or 6.1 mg/kg/d in males and 0, 3.9, 5.8, or 7.5 mg/kg/d in females)	Parental NOAEL = not established Parental LOAEL = 2.9/3.9 mg/kg/d (M/F) based on decreased plasma, erythrocyte and brain cholinesterase activity Offspring NOAEL = not established Offspring LOAEL = 2.9/3.9 mg/kg/d based on decreased plasma, erythrocyte and brain cholinesterase activity and decreased body weight
870.4100a	Chronic Toxicity (rat)	See 870.4300	See 870.4300
870.4100b	Chronic Toxicity (dog)	41939801, 42192301 (1990) 0, 5, 20, or 125 ppm (0, 0.18, 0.70, or 4.18 mg/kg/d in males and 0, 0.19, 0.76, or 4.31 mg/kg/d in females) Acceptable/guideline	Cholinesterase NOEL = not established Cholinesterase LEL = 0.18 mg/kg/d based on decreased brain cholinesterase. Additionally, RBC cholinesterase decreased in the mid- and high-dose groups and plasma cholinesterase decreased in the high-dose group. Systemic NOEL = not established Systemic LEL = 0.18 mg/kg/d based on decreased liver weights in females and presence of a brown, granular pigment in the liver of both sexes. Decreased heart weights in the high-dose group.
870.4200a	Carcinogenicity (rat)	See 870.4300	See 870.4300
870.4200b	Carcinogenicity (mouse)	00163800 (1986) 0, 25, 100 or 200 ppm (0, 3.75, 15 or 30 mg/kg/d) Acceptable/guideline	Cholinesterase NOEL= not established Cholinesterase LEL = 3.75 mg/kg/d based on decreased plasma and erythrocyte cholinesterase. No brain cholinesterase measurements taken. Systemic NOEL = not established Systemic LEL = 3.75 mg/kg/d based on cholinesterase depression in both sexes and hepatocytic vacuolization in female mice Liver tumors in female mice and lung and hemolymphoreticular system tumors in male mice observed at 30 mg/kg/d

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300	Combined Chronic Toxicity/ Carcinogenicity (rat)	00164177 (1986) 0, 1, 5, 25 or 100 ppm (0, 0.05, 0.25, 1.25, or 5 mg/kg/d) Acceptable/guideline	Cholinesterase NOEL = 0.05 mg/kg/d Cholinesterase LEL = 0.25 mg/kg/d based on decreased brain and RBC holinesterase activity Systemic NOEL = 1.25 mg/kg/d Systemic LEL = 5 mg/kg/d based on increased mortality (females), anemia (males) and increased leukocytes (both sexes) In males only, dose-related trends for spleen hemangiosarcomas, spleen hamangiomas/hemangiosarcomas combined, and combined spleen hemagniomas/hemangiosarcomas and skin hemangiosarcomas. Additionally, there were increases in the incidences of spleen hemangioma/hemangiosarcomas combined and of angiogenic tumors at all sites in high dose males.
870.5100	Bacterial reverse mutation	00063996 (1977) Acceptable	Dimethoate and isodimethoate classified as non-mutagenic
870.5300	*In vitro* mammalian cell gene mutation	00151223(1985) Acceptable	Compound-related increases in mutant frequency (MF) were considered equivocal (technical problems with assay and increased MFs did not exceed normal background rates of mutation)
870.5385	*In vivo* bone marrow cytogenetics (rat)	00150579 (1985) Acceptable	No clastogenic response up to 150 mg/kg
870.5395	Mammalian micronucleus (mouse)	00146521 (1985) Acceptable	Did not induce any significant increase in the number of polychromatic erythrocytes (PCE) containing micronuclei with single or multiple doses of 55 mg/kg
870.5450	Dominant Lethal Assay (mouse)	00150578 (1985) Acceptable	No clastogenic response up to 20 mg/kg/d
870.5500	Unscheduled DNA synthesis (UDS) in mammalian cells	43151801 (1990) Acceptable	Positive for inducing UDS in rat hepatocytes exposed to 763.33 ug/ml and above Positive for inducing UDS in rat hepatocytes exposed to doses up to the highest dose tested of 2290 ug/ml
870.6100	Acute Delayed Neurotoxicity (hen)	42884401 (1991) Acceptable/guideline	No clinical signs of acute delayed neurotoxicity and no compound-related histological changes in nerve tissue

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.6200a	Acute Neurotoxicity Screening Battery (rat)	42865102 (1993) 0, 2, 20, or 200 mg/kg Acceptable/guideline	Systemic NOEL = 20 mg/kg Systemic LEL = 200 mg/kg based on decreased body weight Neurotoxicity NOEL = 2 mg/kg Neurotoxicity LEL = 20 mg/kg based on pupil response. At highest dose tested, additional effects were observed including tremors, decreased motor activity, decreased body temperature, increased catalepsy time and eleven other parameters which indicated coordination, sensory and motor systems were affected
870.6200b	Subchronic Neurotoxicity Screening Battery (rat)	43128201 (1994) 0, 1, 50 or 125 ppm (0, 0.06, 3.22, or 8.13 mg/kg/d for males and 0, 0.08, 3.78 or 9.88 mg/kg/d for females) Acceptable/guideline	Cholinesterase NOEL = 0.06/0.08 mg/kg/d (M/F) Cholinesterase LOEL = 3.22/3.78 mg/kg/d (M/F) based on decreased cholinesterase activity in the plasma and RBCs. Brain cholinesterase activity reduced at the highest dose tested.
870.6300	Developmental Neurotoxicity (rat)	45529703 (2001) 0, 0.1, 0.5, or 3 mg/kg/d Acceptable/guideline	Maternal NOAEL = 3 mg/kg/d Maternal LOAEL = not established Offspring NOAEL = 0.1 mg/kg/d Offspring LOAEL = 0.5 mg/kg/d based on increased pup death and increased motor activity (horizontal activity)
870.7485	Metabolism and Pharmacokinetics	43964001 (1995) Acceptable - Single oral dose (10 or 100 mg/kg) of ^{14}C-dimethoate - Intravenous dose (10 mg/kg) of ^{14}C-dimethoate - 14 day repeated oral dose of dimethoate followed by single oral dose of ^{14}C-dimethoate	No sex-, dose- or treatment-related differences in the absorption, distribution, and elimination of dimethoate. Tmax reached less than 1 hour post-dosing. Total recovery of radioactivity ranged 91-97% of the administered dose. Most of the radioactivity was excreted via the urine (85-91% of the dose). A small amount of radioactivity was found in feces (1-2% of the dose), in the tissues and remaining carcass (1-2% of the dose), and in the expired air as carbon dioxide (2-3% of the dose). Dimethoate is metabolized via hydrolytic and oxidative pathways (based on urine analyses). Metabolites include dimethoate carboxylic acid, dimethyldithiophosphate, dimethylthiophosphoric acid, dimethylphosphoric acid, and the oxon analogue, omethoate.
870.7485	Metabolism and Pharmacokinetics	46497601(2004)	A metabolism study with human volunteers was evaluated; however, due to the limitations of the study, including a limited number of subjects and only one dose, it was not useful for dose-response evaluation and not reliable for risk assessment.

Table A.2.3. Subchronic, Chronic, and Other Toxicity Profile - Dimethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.7600	Dermal Absorption	43964001 Acceptable 10 or 100 mg/kg	Dermal absorption (based on a total amount of radioactivity recovered from urine, tissues, and feces) was 8-11% and 1-2% of the administered dose from rats treated at 10 and 100 mg/kg, respectively. No marked sex-related difference was observed in the absorption patterns. The amount of radioactivity recovered from skin wash, extracts from dressing, and treated skin was 62-84%, 1.4-3.6%, and 2-17% of the administered dose, respectively. Total recovery of radioactivity ranged between 89-93% of the administered dose for all tested groups within 5 days after dosing.
870.7600	Dermal Absorption	45530501 Acceptable/guideline 0.02, 0.4 and 4.0 mg/cm^2	Results from the high dose not included because excessive amount of applied material found on the application site cover and surrounding skin. At low- (0.67 mg/kg) and mid-dose (13.3 mg/kg) levels, dermal absorption (based on excreta, cage wash, and carcass) was 6% after 1 hr and ranged from 25-38% at 10 and 24 hours.
870.7800	Immunotoxicity	48572807, 48997901 (2011) Acceptable/guideline 0, 5, 25, 75, or 200 ppm (0, 1, 5, 14.2, or 36.4 mg/kg/d)	Systemic NOAEL = not established Systemic LOAEL = 1 mg/kg/d based on decreased brain cholinesterase levels Immunotoxicity NOAEL = 36.4 mg/kg/d Immunotoxicity LOAEL = not established
Special Studies			
	Cross-fostering Study	46214501 (2004) Acceptable/non-guideline 0, 3, or 6 mg/kg/day	Maternal NOAEL = not established Maternal LOAEL = 3 mg/kg/day based on clinical observations of forelimb hair loss and increased incidences of restlessness and scattering of pups Offspring NOAEL = not established Offspring LOAEL = 3 mg/kg/day based on reduced milk consumption, increased levels of urea in the blood, and increased mortality Direct pre- and post-natal toxicity of the offspring to dimethoate could not be disregarded as significant contributing factors to overall mortality
	Comparative Cholinesterase Study	45529702 (2001) Acceptable/non-guideline 0, 0.1, 0.5, or 3.0 mg/kg/d	Acute NOAEL = 0.5 mg/kg/day Acute LOAEL = 3.0 mg/kg/day based on decreased blood, RBC and plasma cholinesterase Repeated NOAEL = 0.1 mg/kg/day Repeated LOAEL = 0.5 mg/kg/day based on decreased brain cholinesterase

Table A.2.4. Subchronic, Chronic, and Other Toxicity Profile - Omethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3200	21-Day Dermal Toxicity (rat)	46099804 (1979) Unacceptable 0, 2.5, or 20 mg/kg/day	Systemic and dermal NOAEL = 20 mg/kg/day Systemic and dermal LOAEL = not established Cholinesterase NOAEL = not established Cholinesterase LOAEL = 2.5 mg/kg/day based on inhibition of brain cholinesterase activity in females Deficiencies: only 2 dose groups, no dose selection rationale, lack of details regarding substance preparation, age of rabbits and acclimation period not provided, analyses for homogeneity, stability and concentration were not performed, food consumption was not measured, neurological testing and opthalmological exams were not performed, and lack of measurements for recommended hematology and clinical chemistry parameters
870.3465	Subchronic Inhalation Study (rat)	46358601 (1979) Acceptable/non-guideline 0, 0.96, 2.3 or 7.5 mg/m^3	NOAEL = not established LOAEL = 0.96 mg/m^3 based on depressed cholinesterase activity in brain (males) and RBCs (both sexes)
870.3700a	Prenatal Developmental in Rodent (rat)	46099806 (1990) Acceptable/guideline 0, 0.3, 1.0 or 3.0 mg/kg/day	Maternal NOAEL = 0.3 mg/kg/day Maternal LOAEL = 1.0 mg/kg/day based on body weight decrements Developmental NOAEL = 1.0 mg/kg/d Developmental LOAEL = 3.0 mg/kg/d based on decreased placental weights
870.3700b	Prenatal Developmental in Non-Rodent (rabbit)	46099807 (1990) Acceptable/guideline 0, 0.2, 1.0, or 5.0 mg/kg/day	Cholinesterase NOAEL = 0.2 mg/kg/d Cholinesterase LOAEL = 1 mg/kg/d based on inhibition of RBC and brain cholinesterase activity Maternal NOAEL = 0.2 mg/kg/d Maternal LOAEL = 1 mg/kg/d based on body weight decrements Developmental NOAEL = 0.2 mg/kg/d Developmental LOAEL = 1 mg/kg/d based on increased number of resorptions, increased post-implantation loss and increased incidence of arthrogryposis and epignathus

Table A.2.4. Subchronic, Chronic, and Other Toxicity Profile - Omethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800	Reproduction and Fertility Effects (rat)	46195301 (1981) Unacceptable 0, 0.05, 0.15, or 0.5 mg/kg/day	Parental NOAEL = 0.5 mg/kg/d Parental LOAEL = not established Reproductive NOAEL = 0.15 mg/kg/day Reproductive LOAEL= 0.5 mg/kg/day based on slight reductions in the gestation indices during the second mating of F_0 and F_1 females Offspring NOAEL = 0.05 mg/kg/day Offspring LOAEL = 0.15 mg/kg/day based on decreased in body weight and survival indices
870.3800	Reproduction and Fertility Effects (rat) Exposure through drinking water	45806201 (1992), 46099802 (1994) Acceptable/guideline 0, 0.5, 3.0, or 18 ppm	Parental NOAEL = not established Parental LOAEL = 0.5 ppm based on decreased brain cholinesterase activity Reproductive NOAEL = 3 ppm Reproductive LOAEL = 18 ppm based on decreased fertility and conception rates, increased precoital interval, decrease in the number of pups/litter and lesions of the epididymal epithelium (P and F_1 males) Offspring NOAEL = 3 ppm Offspring LOAEL = 18 ppm based on decreased body weight and reduced survival
870.4100b	Chronic Toxicity (dog)	46099805 (1984) Supplemental/guideline 0, 0.025, 0.125, or 0.625 mg/kg/day	Systemic NOAEL = 0.625 mg/kg/day Systemic LOAEL = not established Cholinesterase NOAEL = 0.025/0.125 mg/kg/day (M/F) Cholinesterase LOAEL = 0.125/0.625 mg/kg/day (M/F) based on inhibition of brain and erythrocyte cholinesterase activity
870.4200a	Carcinogenicity (rat) Feeding study	46119402 (1979) Unacceptable 0, 0.015, 0.05, 0.15, or 0.5 mg/kg/day	Cholinesterase NOAEL = 0.05 mg/kg/day Cholinesterase LOAEL = 0.15 mg/kg/day based on inhibition of cholinesterase activity in the brain, erythrocytes and plasma Systemic NOAEL = 0.5 mg/kg/day Systemic LOAEL = not established Deficiencies: lack of homogeneity and stability data, weekly clinical examination, eye examinations, serum electrolyte measurements, and tabulation of microscopic lesions; animals could have tolerated a higher dose

Table A.2.4. Subchronic, Chronic, and Other Toxicity Profile - Omethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.4200b	Carcinogenicity (mouse) Exposure through drinking water	46126002 (2001) Acceptable/guideline 0, 0.5, 4 or 32 ppm (0, 0.10, 0.82, or 6.48 mg/kg/day in males and 0, 0.11, 0.80, 6.61 mg/kg/day in females)	Cholinesterase NOAEL = 0.5 ppm Cholinesterase LOAEL = 4 ppm based on decreased cholinesterase activity in plasma, erythrocytes, and brain Systemic NOAEL = 4 ppm Systemic LOAEL = 32 ppm based on tremors in both sexes No significant increase in neoplasms
870.4300	Combined Chronic Toxicity/ Carcinogenicity (rat) Exposure through drinking water	46126001 (1995) Acceptable/guideline 0, 0.5, 4 or 32 ppm (0, 0.04, 0.30, or 2.92 mg/kg/day in males and 0, 0.05, 0.44, or 3.93 mg/kg/day in females)	Cholinesterase NOAEL = not established Cholinesterase LOAEL = 0.5 ppm based on inhibition of erythrocyte cholinesterase activity in males. At 4 ppm, brain and erythrocyte activity decreased in both sexes. Plasma activity decreased at the highest dose tested. Systemic NOAEL = 4 ppm Systemic LOAEL = 32 ppm based on transient decreases in body weight, clinical signs indicative of neurotoxicity, and lesions in the eyes and forestomach in both sexes; vacuolation of the epididymal epithelium in males; mammary gland hyperplasia in females
870.5100	Mammalian Activation Gene Mutation Assay	46098604 (1988) Acceptable/guideline	No evidence of induced mutant colonies
870.5300	*In vitro* mammalian cell gene mutation	46098612 (1988) Acceptable/guideline	Strong evidence of a concentration related positive response of sister chromatid exchange induced over background; statistically and biologically significant ≥1700 µg/ml
870.5385	*In vivo* bone marrow cytogenetics (mice)	46098608 (1988) Acceptable/guideline	No statistically significant increase in frequency of micronucleated PCE
870.5450	Dominant Lethal Assay (mouse)	46098605 (1991) Unacceptable	No response up to 20 mg/kg/d Deficiency: no concurrent positive control data
870.5500	Unscheduled DNA synthesis in mammalian cells	46098613 (1989) Acceptable/guideline	No evidence of unscheduled DNA synthesis up to 30 mg/kg
870.5550	Unscheduled DNA synthesis in rat hepatocytes	46098603 (1989) Acceptable/guideline	Evidence of dose related positive response; unscheduled DNA synthesis induced at dose levels ≥256 µg/ml
870.5915	*In vivo* cytogenetic mutagenicity	46098607 (1990) Acceptable/guideline	No evidence of sister chromatid exchange (SCE) induction up to 20 mg/kg/day
870.6100	Acute Delayed Neurotoxicity (hen)	46099801(1993) Acceptable/non-guideline 140 mg/kg	No treatment-related pathological changes in nerve tissues

Table A.2.4. Subchronic, Chronic, and Other Toxicity Profile - Omethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.6200a	Acute Neurotoxicity Screening Battery (rat)	46167701 (2003) Acceptable/guideline 0, 0.2, 0.25, 0.35, or 5 mg/kg	ChE NOAEL = 0.25 mg/kg ChE LOAEL = 0.35 mg/kg Systemic NOAEL = 0.2 mg/kg Systemic LOAEL = 0.25 mg/kg based on FOB effects
870.7485	Metabolism and Pharmacokinetics	46099808	Male and female rats exhibited signs of toxicity at 0.5-4 hrs post-dosing including trembling, salivation, high breathing rate, and congestion of the eyes. Overall recovery of administered radioactivity was 88-98%. There were no remarkable sex-, dose- or treatment-related differences in the absorption, distribution, and elimination of omethoate. Absorption rates were rapid and T_{max} was reached within 1 hour post-dosing. Omethoate was rapidly excreted within 48 hours with the majority excreted via the urine (85-97% of the administered dose). The remainder of the administered radioactivity was excreted via the feces (2-4% of the administered dose). Biliary excretion was found to account for the majority of the fecal metabolite content. Based upon tissue burden data, omethoate and/or its metabolites do not appear to undergo any significant sequestration. Omethoate appeared to be metabolized to a greater extent in males than in females.
Special Studies			
	Investigation of Effects on Long-Term Cholinesterase Activity Exposure through drinking water for 32 weeks	46099816 (1994) Acceptable/non-guideline 0, 100 or 300 ppb	Designed to determine a drinking water dose that would result in no inhibition of RBC, plasma or brain cholinesterase activity in young adult rats. No cholinesterase inhibition was observed in any examined compartment for all doses.
	Cholinesterase Activity (dog) Gavage for 13 weeks	46099814 (1991) Acceptable/non-guideline 0 or 0.0125 mg/kg/day	No inhibition of cholinesterase activity
	In vivo mammalian gene mutation – spot test in mice	46098606 (1990) Acceptable/non-guideline 0, 4, 8, or 16 mg/kg/day	Statistically significant, dose-dependent increase in number of relevant F1 coat spots in dose groups

Table A.2.4. Subchronic, Chronic, and Other Toxicity Profile - Omethoate			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
	Acute Comparative Cholinesterase Assay	48779401 (2012) 0, 0.1, 0.3, 0.6, or 0.9 mg/kg	NOAEL for RBC cholinesterase inhibition=0.1 mg/kg LOAEL for RBC cholinesterase inhibition=0.3 mg/kg NOAEL for brain cholinesterase inhibition = 0.1 mg/kg LOAEL for brain cholinesterase inhibition = 0.3 mg/kg

Appendix B. Summary of OPP's Cholinesterase Policy & Use of BMD Modeling

OPP's cholinesterase (ChE) policy (USEPA, 2000[18]) describes the manner in which ChE data are used in human health risk assessment. The following text provides a brief summary of that document to provide context to points of departure selected.

AChE inhibition can be inhibited in the central or peripheral nervous tissue. Measurements of AChE or ChE inhibition in peripheral tissues (e.g., liver, diaphragm, heart, lung, etc.) are rare. As such, experimental laboratory studies generally measure brain (central) and blood (plasma and RBC) ChE. Blood measures do not represent the target tissue, *per se*, but are instead used as surrogate measures for peripheral toxicity in studies with laboratory animals or for peripheral and/or central toxicity in humans. In addition, RBC measures represent AChE, whereas plasma measures are predominately butyryl-ChE (BuChE). Thus, RBC AChE data may provide a better representation of the inhibition in target tissues. As part of the dose response assessment, evaluations of neurobehavior and clinical signs are performed to consider the dose response linkage between AChE inhibition and apical outcomes.

Refinements to OPP's use of ChE data have come in the implementation of BMD approaches in dose response assessment. Beginning with the OP CRA, OPP has increased its use of BMD modeling to derive PODs for AChE inhibiting compounds. Most often the decreasing exponential empirical model has been used.

OPP does have not a defined BMR for OPs. However, the 10% level has been used in the majority of dose response analyses conducted to date. This 10% level represents a 10% reduction in AChE activity (i.e., inhibition) compared to background (i.e., controls). Specifically, the BMD_{10} is the estimated dose where ChE is inhibited by 10% compared to background. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}.

[18] USEPA (2000) Office of Pesticide Programs, US Environmental Protection Agency, Washington DC 20460. August 18, 2000 Office of Pesticide Programs Science Policy of The Use of Data on Cholinesterase Inhibition for Risk Assessments of Organophosphorous and Carbamate Pesticides.

The use of the 10% BMR is derived from a combination of statistical and biological considerations. A power analysis was conducted by ORD on over 100 brain AChE datasets across more than 25 OPs as part of the OP CRA (USEPA, 2002). This analysis demonstrated that 10% is a level that can be reliably measured in the majority of rat toxicity studies. In addition, the 10% level is generally at or near the limit of sensitivity for discerning a statistically significant decrease in ChE activity in the brain compartment and is a response level close to the background brain ChE level. With respect to biological considerations, a change in 10% brain AChE inhibition is protective for downstream clinical signs and apical neurotoxic outcomes. With respect to RBC AChE inhibition, these data tend to be more variable than brain AChE data. OPP begins its BMD analyses using the 10% BMR for RBC AChE inhibition but BMRs up to 20% could be considered on a case-by-case basis as long as such PODs are protective for brain AChE inhibition, potential peripheral inhibition, and clinical signs of neurotoxicity.

Appendix C. Summary Tables of Benchmark Dose (BMD) Analyses in Rat Toxicity Studies

New studies or studies used as points of departure were analyzed using the most recent version of EPA's Benchmark Dose Software (Version 2.4). Results and technical details for these analyses can be found in the latest BMD analysis memo (M. Perron; 15-SEP-2015; TXR# 0057249). All other results were obtained using previous versions of the modeling software and reported in previous risk assessments.

Table C.1. Summary of BMD Results Following Acute Exposures to Dimethoate.

Study	Age	Compartment	Males		Females	
			BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)	BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)
Comparative Cholinesterase Assay (MRID 48779401)	Adult	Brain	2.52	1.74	2.2	1.3
	Offspring (PND11)	Brain	1.77	1.47	1.55	0.91

Table C.2. Summary of BMD Results Following Acute Exposures to Omethoate.

Study	Age	Compartment	Males		Females	
			BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)	BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)
Comparative Cholinesterase Assay (MRID 45529702)	Adult	Brain	0.15	0.12	0.25	0.20
	Offspring (PND11)	Brain	0.16	0.14	0.16	0.15
	Adult	RBC	0.19	0.16	0.22	0.14
	Offspring (PND11)	RBC	0.13	0.11	0.14	0.13
Acute Neurotoxicity Study (MRID 46167701)	Adult	Brain	0.26	0.17	0.18	0.11

Table C.3. Summary of BMD Results Following Repeated Exposures to Dimethoate.

Study	Age	Compartment	Males		Females	
			BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)	BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)
Comparative Cholinesterase Assay (MRID 48779401)	Fetal (GD20)	Brain	N/A	N/A	0.89	0.70
	Dams (GD20)	Brain	N/A	N/A	0.34	0.28
	Offspring (PND4)	Brain	NF	NF	NF	NF
	Offspring (D21)	Brain	0.39	0.32	0.54	0.44
	Adult (D11)	Brain	0.49	0.37	0.37	0.27
28-day Rat Oral Toxicity Study (MRID 46288001)	Adult	Brain	1.0	0.8	0.8[a]	0.7[a]
DNT Range-Finding (MRID 45529701)	Dams (GD20)	Brain	N/A	N/A	0.2	0.2
	Fetus (GD20)	Brain	1.0	0.3	1.0	0.4
	Offspring (PND21)	Brain	0.4	0.3	0.5	0.4
Two-generation Reproduction Toxicity Study (MRID 42251501)	Adult (P generation; day 224)	Brain	0.7	0.7	0.3	0.3
	Adult (F_1 generation; day 308)	Brain	0.4	0.3	0.4	0.3
Two-generation Reproduction	Adult (P generation; day 205)	Brain	0.3	0.2	0.5	0.3

Table C.3. Summary of BMD Results Following Repeated Exposures to Dimethoate.

Study	Age	Compartment	Males		Females	
			BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)	BMD_{10} (mg/kg/day)	$BMDL_{10}$ (mg/kg/day)
Toxicity Study (MRID 46181001)	Adult (F_1 generation; day 218)	Brain	0.8	0.4	0.6[a]	0.5[a]
One-generation Reproduction Toxicity Study (MRID 46348201)	Adult (P generation; day 91)	Brain	0.4	0.3	0.5	0.4
	Adult (F_1 generation; day 42)	Brain	0.3[a]	0.2[a]	0.4	0.3
Chronic Oral Toxicity Study (MRID 00164177)	Adult	Brain	0.25[b]	0.22[b]	-	-
Dermal Toxicity Study (MRID 44999101)	Adult	Brain	31.3	24.8	28.5	20.2

N/A = not applicable; NF = no reliable fit.
[a] Noted as having a poor model fit.
[b] Value calculated using both sexes and all time points from the chronic oral toxicity study for the OP CRA (2002, 2006).

Table C.4. Summary of BMD Results Following Repeated Exposures to Omethoate.

Study	Age	Compartment	Males		Females	
			BMD_{10} (mg/m^3/day)	$BMDL_{10}$ (mg/m^3/day)	BMD_{10} (mg/m^3/day)	$BMDL_{10}$ (mg/m^3/day)
Omethoate Inhalation Toxicity Study (MRID 46358601)	Adult	Brain	0.51	0.38	1.24	1.05

Appendix D. Tolerance Summary for Dimethoate

Table D.1. Tolerance Summary for Dimethoate (40 CFR §180.204).

Commodity	Established Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
(a) *General.*			
Alfalfa, forage	2.0	2.0	
Alfalfa, hay	2.0	2.0	
Alfalfa, seed	-	4.0	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Bean, dry, seed	2.0	2.0	
Bean, lima	2.0	2.0	Bean, lima, succulent
Bean, snap, succulent	2.0	2.0	
Blueberry[1]	1.0	1.0	
Broccoli	2.0	2.0	
Cattle, meat byproducts	0.02	0.10	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Cauliflower	2.0	2.0	
Celery	2.0	2.0	
Citrus, dried pulp	5.0	5.0	
Corn, field, forage	1.0	1.0	
Corn, field, grain	0.1	0.10	
Corn, field, stover	1.0	1.0	
Corn, pop, grain	0.1	0.10	
Corn, pop, stover	1.0	1.0	
Corn, sweet, forage	1.0	-	Revoke- no registered use on sweet corn
Cotton, undelinted seed	0.1	0.10	
Cotton, gin byproducts	-	4.0	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Egg	0.02	-	Revocation recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Endive	2.0	2.0	
Fruit, citrus, group 10-10	-	2.0	Crop group tolerance is being established rather than individual tolerances
Goat, meat byproducts	0.02	0.10	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Grapefruit	2.0	-	Delete individual commodities and establish group 10-10 tolerance
Hog, meat byproducts	0.02	0.10	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Horse, meat byproducts	0.02	0.10	
Kale	2.0	2.0	
Lemon	2.0	-	Delete individual commodities and establish group 10-10 tolerance
Lettuce, leaf	2.0	2.0	
Melon	1.0	1.0	
Milk	0.002	0.002	

Table D.1. Tolerance Summary for Dimethoate (40 CFR §180.204).			
Commodity	Established Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
Mustard greens	2.0	2.0	
Orange	2.0	-	Delete individual commodities and establish group 10-10 tolerance
Pea	2.0	2.0	
Pear	2.0	2.0	
Pecan	0.1	0.10	
Pepper	2.0	2.0	
Potato	0.2	0.20	
Poultry, meat byproducts	0.02	-	Revocation recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Safflower, seed	0.1	0.10	
Sheep, meat byproducts	0.02	0.10	Recommended in Memo M. Sahafeyan D232849; 24-MAY-2011
Sorghum, grain, forage	0.1	0.10	
Sorghum, grain, grain	0.1	0.10	
Sorghum, grain, stover	0.1	0.10	
Soybean, forage	2.0	2.0	
Soybean, hay	2.0	2.0	
Soybean, seed	0.05	0.05	
Swiss chard	2.0	2.0	
Tangerine	2.0	-	Delete individual commodities and establish group 10-10 tolerance
Tomato	2.0	2.0	
Turnip, roots	0.2	0.20	
Turnip, tops	2.0	2.0	
Wheat, grain	0.04	0.05	Harmonize with Codex MRL
Wheat, hay	2.0	2.0	
Wheat, straw	2.0	2.0	
Wheat, forage	2.0	2.0	
(c) *Tolerances with regional registrations.*			
Asparagus	0.15	0.15	
Brussels sprouts	5.0	5.0	
Cherry, sweet	2.0	2.0	
Cherry, tart	2.0	2.0	
Grass, forage	-	0.05	Recommended in Memo M. Sahafeyan D239886; 12-NOV-2013
Grass, hay	-	0.05	

[1] There are no U.S. registrations as of August 16, 1996.

Appendix E. Physical/Chemical Properties

Table E.1. Physical/Chemical Properties of Dimethoate.

Parameter	Value	Reference
Molecular Weight	229.25 g mol	
pH	3.39	MRID# 48696601
Water solubility (25°C)	39.8 g/L	MRID# 48696601
Solvent solubility (25°C)	140 g/100 mL acetone 140 g/100 mL acetonitrile 120 g/100 mL cyclohexanone 0.043 g/100 mL dodecane 150 g/100 mL ethanol 120 g/100 mL ethyl acetate 0.030 g/100 mL hexane 120 g/100 mL 2-propanol 160 g/100 mL methanol 150 g/100 mL dichloromethane 52 g/100 mL 1-octanol 100 g/100 mL toluene 31 g/100 mL xylenes 120 g/100 mL 1,2-dichloroethane 0.024 g/100 mL n-heptane	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation98/dimetho.PDF
Vapor pressure (25°C)	1.85×10^{-6} mPa	MRID# 48696601
Octanol/water partition coefficient, log K_{OW}	0.70	MRID# 48696601
UV/Vis absorption	The mean molar absorption coefficient and mean bandwidth for pH 7.10 (at 203.0 ± 0.0 nm) were determined to be 7661 L/mol-cm and 16.5 nm.	MRID# 47622901

Appendix F. Use Summary for Dimethoate

Table F.1. Summary of Registered Labels for Dimethoate.

Product Name/Formulation	Registration No
Gowan Dimethoate E267	10163-56
Drexel Dimethoate 4EC	19713-231
Drexel Dimethoate 2.67	19713-232
Dimethoate 400	34704-207
Dimethoate 2.67 EC	34704-489
Dimethoate 4E	66330-223
Dimethoate 25 WP	66330-237
Dimethoate 2.67 EC	66330-244
Cymate 267	66330-245
Dimethoate 400	67760-118
Dimethoate 4E	67760-44
Agrisolutions Dimate 4E	9779-273
Clean Crop Dimethoate 400	CA970003
Dimethoate 4E	ID110008
Dimethoate 400	ID120004
Clean Crop Dimethoate 400	ID980006
Dimethoate 400	OR050019

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Agricultural uncultivated areas (Noncropland adjacent to vineyards)	Groundboom/ Handgun application	Liquid	2 lb ai/A 0.0025 lb ai/gal (Mech HG)	NS	NS	2 per year	NS	NS
Alfalfa (field and seed crop)	Aerial, Groundboom, Chemigation	Liquid	0.5 lb ai/A	0.5 lb ai/A	NS 30	1 per crop cycle or cutting; 3 per year	48 hours	10
Asparagus	Aerial, Groundboom, Chemigation	Liquid	0.5 lb ai/A	1 lb ai/A	NS 14	2	48 hours	180
Beans (fresh, snap, lima, dry, not cowpeas)	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	NS 14	2	48 hours	NS 0 2
Broccoli, Cauliflower	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	1.5 lb ai/A	7	3	48 hours; increased to 72 hours in outdoor areas where the average annual rainfall is less than 25 inches per year.	7
Brussel sprouts	Aerial, Groundboom, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A[a]	1.5 lb ai/A	7	3	48 hours; increased to 72 hours in outdoor areas where the average annual rainfall is less than 25 inches per year.	10
Celery	Aerial, Groundboom, Chemigation	Liquid	0.5 lb ai/A	1.5 lb ai/A	7	3	48 hours	7
Cherries (preharvest and postharvest)	Aerial, Airblast, Chemigation	Liquid	1.33 lb ai/A	1.33 lb ai/A	NS	NS	10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year.	21[b]
Christmas tree nurseries	Aerial, Airblast, Chemigation, Handheld; Soil injectors (some labels restrict aerial and chemigation)	Liquid	1 lb ai/A 0.025 lb ai/gal 0.0025 lb ai/gal (Mech HG)	3 lb ai/A	14	3	10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year	NA

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Citrus - non-bearing and nursery stock	Aerial, Airblast, Chemigation, Handheld (some labels restrict aerial and chemigation)	Liquid	1 lb ai/A foliar spray: 0.005 lb ai/gal 0.0025 lb ai/gal (Mech.HG) soil drench: 2 lb ai/A	1 lb ai/A	NS	NS	10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year	NA
Citrus (grapefruit, kumquat, lemons, limes, oranges pummelo, tangelo, and tangerines)	Aerial, Airblast, Chemigation, Handheld (some labels restrict aerial and chemigation)	Liquid	1 lb ai/A	1 lb ai/A	NS	NS no more than 2 apps to mature fruit	10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year	15-45 (depending on pest)
Corn (field and popcorn)	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	0.5 lb ai/A	NS	NS 3	48 hours; 4 days for detasseling tasks in non-arid areas and 15 days in outdoor areas where the average annual rainfall is less than 25 inches per year.	14[c] 14 (forage) 14 (grain) 28 (grain) 28 (forage) 42 (grain)
Cotton	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	14 14 when water is used for dilution; 40 when once refined vegetable oil is used for dilution.	2	48 hours	14

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Endive, Leaf lettuce, Swiss chard	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.25 lb ai/A	0.75 lb ai/A	7	3	48 hours	14
Garbanzo beans	Aerial, Groundboom, Chemigation	Liquid	0.5 lb ai/A	1 lb ai/A	14	2	48 hours	0 2
Grass grown for seed	Aerial, Groundboom, Chemigation	Liquid	0.5 lb ai/A	1 lb ai/A	90	NS	48 hours	NS 14
Kale	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.25 lb ai/A (Label 66330-244: indicates 1.5 pt/A = 0.5 lb ai/A)	0.5 lb ai/A	15	2	48 hours	14
Lentils	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	NS 7	2	48 hours	0 2 14
Lupine	Aerial, Groundboom, Chemigation, Handheld	Liquid	0.5 lb ai/A 0.0025 lb ai/gal (Mech HG)	1 lb ai/A	14	2	48 hours	0
Melons	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	NS 7	NS 2	48 hours	3
Mustard greens	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.25 lb ai/A	0.5 lb ai/A	9	2	48 hours	14

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Ornamentals in outdoor nurseries	Aerial, Airblast, Chemigation, Handheld; Soil injectors (some labels restrict aerial and chemigation)	Liquid	4.15 lb ai/A (airblast) 1 lb ai/A 0.08 lb ai/gal 0.0025 lb ai/gal (Mech.HG) soil drench: 0.06 lb ai/gal and 5.5 lb ai/A soil injection: 0.004 lb ai/inch of tree circumference	4.15 lb ai/A (airblast only) 3 lb ai/A	14	3	woody ornamentals: 10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year herbaceous ornamentals: 48 hours conifer seed orchards: 48 hours (16 days if airblast >1 lb ai/A); increased to 4 days (25 days if airblast >1 lb ai/A) in outdoor areas where the average annual rainfall is less than 25 inches per year	NA
Ornamentals in outdoor nurseries (trees grown for pulp -- forestry)	Aerial, Airblast, Chemigation, Handheld; Soil injectors	Liquid	2 lb ai/A 0.04 lb ai/gal 0.0025 lb ai/gal (Mech HG) soil injection: 0.0025 lb ai/inch tree circumference	6 lb ai/A	NS	3	14 days; increased to 24 days in outdoor areas where the average annual rainfall is less than 25 inches per year.	NA
Pears (including non-bearing and nursery stock)	Aerial, Airblast, Chemigation, Handheld (some labels restrict chemigation)	Liquid	1 lb ai/A 0.005 lb ai/gal; 0.0025 lb ai/gal (Mech HG)	1 lb ai/A	NS	NS	10 days; increased to 14 days in outdoor areas where the average annual rainfall is less than 25 inches per year	28
	Aerial, Airblast	WSB	1 lb ai/A	1 lb ai/A				

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Peas	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.16 lb ai/A	0.16 lb ai/A	NS 7	NS	48 hours	0 2
Peas (dry; some labels limit to those in ID, OR and WA only)	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.33 lb ai/A 0.5 lb ai/A (allowed on SLN)	0.5 lb ai/A	NS 7	NS 3[d]	48 hours	0 5-14[d]
Peas (succulent; some labels limit to those in ID, OR and WA only)	Aerial, Groundboom, Chemigation (some labels restrict chemigation)	Liquid	0.33 lb ai/A 0.5 lb ai/A (allowed on SLN)	0.5 lb ai/A	NS 7 14	NS 3[e]	48 hours	NS 5-14[e]
Pecans	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.33 lb ai/A	0.33 lb ai/A	NS	NS	48 hours	21
Peppers	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.33 lb ai/A	1.65 lb ai/A	7	5	48 hours	NS 0 2[f]
Potatoes	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	7	2	48 hours	NS 0 2[g]
	Aerial, Groundboom	WSB						
Safflower	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	0.5 lb ai/A	NS 14	NS 1 2 at lower rate[h]	48 hours	14[h]
Sorghum	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	7	2	48 hours	28

Table F.2. Summary of Use Directions for Dimethoate.

Crop	Applic. Timing, Type, and Equip.	Formulation	Maximum Applic. Rate	Max Seasonal Applic. Rate	RTI (days)	Max No. Apps per Season	REI	PHI (days)
Soybeans	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	7	2	48 hours	21 28[i]
Tomatoes	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	6	2	48 hours	7
Turnip	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.25 lb ai/A	1.75 lb ai/A	3	7	48 hours	14
Watermelon	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	1 lb ai/A	7	2	48 hours	3
Wheat	Aerial, Airblast, Chemigation (some labels restrict aerial and chemigation)	Liquid	0.5 lb ai/A	0.5 lb ai/A	NS	2 (at lower rates)	48 hours	35 45 60

a. Label 67760-118: directions state max of 0.5 lb ai/A, but also indicate 38.2 fl oz/A = 1 lb ai/A.
b. Label 66330-223 lists the PHI as 21 days; but then also says interval b/t last app and harvest is 28 days.
c. Labels listed various PHIs; not clear if which are correct.
d. Max # apps and PHI listed on SLN.
e. Max of 3 apps listed on label 67760-118; PHI listed on SLNs.
f. Labels 66330-244 and 66330-245 list PHI of 2 days.
g. Labels 66330-244 and 66330-245 list PHI of 2 days.
h. A couple of labels (e.g., 34704-489) list RTI of 14 days and no more than two apps.
i. One label (67760-118) listed a longer PHI.

Appendix G. International Residue Limits

(035001; 09/29/14)

Table G.1. Summary of U.S. Tolerances and International MRLs.				
U.S.		**Canada**	**Mexico[1]**	**Codex[2]**
Residue Definition:				
40CFR180.204 (a) *General.* Tolerances are established for total residues of the insecticide dimethoate (*O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorodithioate) including its oxygen analog (*O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorothioate)		*O*,*O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorodithioate, including the metabolite omethoate		Dimethoate
Commodity Tolerance (ppm)/Maximum Residue Limit (mg/kg)				
Commodity	U.S.	Canada	Mexico[1]	Codex[2]
Alfalfa, forage	2.0			
Alfalfa, hay	2.0			
Bean, dry, seed	2.0	1 beans		
Bean, lima	2.0			
Bean, snap, succulent	2.0			
Blueberry[3]	1.0	1		
Broccoli	2.0	2		
Cattle, meat byproducts	0.02			0.05 (*)
Cauliflower	2.0	2		0.2
Celery	2.0	1		0.5
Citrus, dried pulp	5.0			
Corn, field, forage	1.0			
Corn, field, grain	0.1			
Corn, field, stover	1.0			
Corn, pop, grain	0.1			
Corn, pop, stover	1.0			
Corn, sweet, forage	1.0			
Cotton, undelinted seed	0.1			
Egg	0.02			0.05 (*)
Endive	2.0			
Goat, meat byproducts	0.02			
Grapefruit	2.0	1.5 citrus fruits		5 citrus fruits (excluding kumquats)
Hog, meat byproducts	0.02			
Horse, meat byproducts	0.02			
Kale	2.0	2		
Lemon	2.0	1.5 citrus fruits		5 citrus fruits (excluding kumquats)
Lettuce, leaf	2.0	2 lettuce		
Melon	1.0			
Milk	0.002			0.05 (*) milk of cattle, goats and sheep
Mustard greens	2.0			
Orange	2.0	1.5 citrus fruits		5 citrus fruits
Pea	2.0	0.5		1 peas (pods and succulent=immature seeds)

Table G.1. Summary of U.S. Tolerances and International MRLs.				
U.S.		**Canada**	**Mexico[1]**	**Codex[2]**
Pear	2.0	2		1
Pecan	0.1			
Pepper	2.0	0.5		3 peppers Chili, dried 0.5 peppers, sweet (including pimento or pimiento)
Potato	0.2			0.05
Poultry, meat byproducts	0.02			0.05 (*)
Safflower, seed	0.1			
Sheep, meat byproducts	0.02			0.05 (*)
Sorghum, grain, forage	0.1			
Sorghum, grain, grain	0.1			
Sorghum, grain, stover	0.1			
Soybean, forage	2.0			
Soybean, hay	2.0			
Soybean, seed	0.05			
Swiss chard	2.0	2		
Tangerine	2.0	1.5 citrus fruits		5 citrus fruits (excluding kumquats)
Tomato	2.0	0.5		
Turnip, roots	0.2			
Turnip, tops	2.0	2		1 turnip greens
Wheat, forage	2.0			
Wheat, grain	0.04			0.05
Wheat, hay	2.0			
Wheat, forage	2.0			
Wheat, straw	2.0			1 wheat straw and fodder, dry
MRLs with NO US Equivalent				
Artichoke, globe				0.05
Barley				2
Cabbage, savoy		2 cabbages		0.05 (*)
Lettuce, head				0.3
Mammalian fats (except milk fats)				0.05 (*)
Mango				1 Po
Meat of cattle, goats, horses, pigs and sheep				0.05 (*)
Olives				0.5
Poultry, fats				0.05 (*)
Poultry, meat				0.05 (*)
Spices, fruits and berries				0.5
Spices, roots and rhizomes				0.1 (*)
Spices, seeds				5
Sugar beet				0.05
Turnip, garden				
Apples		2		
Garden beet tops		2		
Spinach		2		
Strawberries		1		
Sunflower seeds		0.1		
Completed by: M. Negussie; 10/06/14				

[1]Mexico defers to US tolerances and/or Codex MRLs for its export purposes.

[2] (*) = absent at the limit of quantitation. Po = postharvest treatment, such as treatment of stored grains.
[3] There are no U.S. registrations as of August 16, 1996.

(c) *Tolerances with regional registrations.* Tolerances with regional registration, as defined in §180.1(l), are established for total residues of dimethoate including its oxygen analog in or on the following food commodities:

Commodity	US	Canada	Mexico[1]	Codex[2]
Asparagus	0.15			0.05 (*)
Brussels sprouts	5.0			0.2
Cherry, sweet	2.0	2 cherries		2 cherries
Cherry, tart	2.0			

Appendix H – Summary of Surface Water EDWCs using Maximum and Typical Application Rates

Table H.1. Dimethoate EDWCs (µg/L) for Dimethoate Uses in the U.S. Corrected for National PCA, Using Maximum Application Rates.

PRZM Scenario (bold font)/ Uses Represented	App Method	Date of First Application (DD-MM)	App Rate kg ai/A (lb ai/A)	No. of Apps.	App. Interval (days)	Natl. PCA	EDWCs (µg/L)[1]		
							Acute	Chronic	Cancer/ Chronic
01_CA wine grapes/ Agricultural uncultivated areas (CA only) (Noncropland adjacent to vineyards)	Ground-boom, handgun app.	15-02	2.13 (1.9)	2	180	0.91	24.7	3.26	1.74
03_MN alfalfa/ Alfalfa, Sainfoin	Aerial	20-05	0.560 (0.5)	1/CC 3/year	30	0.91	11.0	1.32	0.928
04_CA cole crops/ Broccoli, Cauliflower; Additionally, Brussels sprouts (aerial, some labels allow use only in CA)	Aerial	25-01	0.560 (0.5)	3	7	0.91	27.3	3.49	1.90
05_CA cole crops/ Brussels sprouts (ground)	Ground	18-01	0.841 (0.75)	2	7	0.91	**43.9**	**5.66**	1.88
06_CA row crops/ Celery	Aerial	05-03	0.560 (0.5)	3	7	0.91	7.37	1.00	0.606
07_FL cabbage/ Turnip (greens)	Aerial	15-01	0.281 (0.251)	7	3	0.91	17.5	1.52	0.983
08_CA potato/ Turnip (roots)	Aerial	01-05	0.281 (0.251)	7	3	0.91	9.19	0.974	0.814
09_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	Aerial	15-10 (pre-harvest)	1.51 (1.35)	1	N/A	0.91	6.77	1.06	1.00
10_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	Aerial	15-11 (post-harvest)	1.51 (1.35)	1	N/A	0.91	6.77	1.16	1.09
10b_WA orchards/ Cherry (only in ID, MT, OR, UT and WA)	Ground	15-11 (post-harvest)	1.51 (1.35)	1	N/A	0.91	3.31	0.586	0.539
20_FL peppers/ Peppers	Aerial	20-10	0.377 (0.336)	5	7	0.91	40.0	2.52	1.21
21_FL peppers/ Peppers	Ground	20-10	0.377 (0.336)	5	7	0.91	39.8	2.39	1.03
22_MI beans/ Beans (includes dry beans, excludes cowpeas), Garbanzos (includes chick peas), Lupine	Aerial	20-07	0.560 (0.5)	2	14	0.91	8.90	0.847	0.578
23_MS Cotton/ Cotton	Aerial	20-07	0.560 (0.5)	2	14	0.91	13.8	0.865	0.480
24_PA Tomato/ Tomato	Aerial	20-09	0.560 (0.5)	2	6	0.91	18.1	1.77	0.919

Table H.1. Dimethoate EDWCs (µg/L) for Dimethoate Uses in the U.S. Corrected for National PCA, Using Maximum Application Rates.

PRZM Scenario (bold font)/ Uses Represented	App Method	Date of First Application (DD-MM)	App Rate kg ai/A (lb ai/A)	No. of Apps.	App. Interval (days)	Natl. PCA	EDWCs (µg/L)[1]		
							Acute	Chronic	Cancer/ Chronic
25_CA citrus/ Grapefruit, Kumquat, Lemon, Lime, Orange, Pummelo (shaddock), Tangelo, Tangerine	Aerial	01-06	1.121 (1)	1	N/A	0.91	5.40	0.389	0.355
26_FL citrus/ Same crops as above	Aerial	01-06	1.121 (1)	1	N/A	0.91	38.9	1.95	0.659
27_ID potatoes/ Potatoes	Aerial	20-08	0.560 (0.5)	2	7	0.91	13.7	1.55	1.26
12_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	Airblast	01-06	5.04 (4.5)	1	N/A	1.0	9.46	0.990	0.927
13_CA forestry/ Cottonwood (forest/ shelterbelt)	Aerial	01-06	2.24 (2)	3	14	1.0	24.8	3.73	**3.68**
14_OR Xmas trees/ Hybrid cottonwood/poplar plantations (some labels allow use in ID, OR and WA)	Aerial	01-06	2.24 (2)	3	10	1.0	26.7	3.40	3.27
15_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	Soil drench	01-06	2.13 (1.9)	1	N/A	1.0	5.13	0.489	0.462
17_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	Aerial	01-06	1.12 (1)	3	14	1.0	20.8	2.44	2.10
18_NJ nursery/ Ornamental herbaceous plants[2]	Soil drench	01-06	7.29 (6.5)	1	N/A	1.0	105[2]	7.66[2]	3.53

Bolded and shaded values are the highest EDWCs.
[1] Concentrations are modified using a national PCA, but not using a TAF. Application rates in kg ai/ha (lb ai/A). EDWCs were rounded to three significant figures.
[2] A maximum rate of 6.5 lb ai/A for this use appears to be a label error; therefore, these results are not considered representative.

Table H.2. Dimethoate EDWCs (µg/L) for Dimethoate Uses in the U.S. Corrected for Regional PCA, Using Typical Application Rates and Numbers of Applications[1]

Scenario (bold font)/ Crops/Uses Represented	App Method	Date of First Application (DD-MM)	Aver. App Rate kg ai/A (lb ai/A)	Aver. Number of Apps	App Interval (days)	Reg. PCA	EDWCs (µg/L)[1]		
							Acute	Chronic	Cancer/ Chronic
03c_MN alfalfa/ Alfalfa	Aerial	20-05	0.409 (0.365)	1 (1.1)	N/A	0.91	3.39	0.345	0.178
04b_CA cole crops/ Broccoli	Aerial	25-01	0.535 (0.477)	1 (1.3)	N/A	0.61	8.97	**0.988**	0.381
22c_MI beans/ Dry beans, peas	Aerial	20-07	0.405 (0.361)	1 (1.1)	N/A	0.81	4.38	0.352	0.162
23c_MS Cotton/ Cotton	Aerial	20-07	0.307 (0.274)	1 (1.2)	N/A	0.86	5.76	0.305	0.107
24b_PA Tomato/ Tomato	Aerial	20-09	0.498 (0.444)	1 (1.3)	N/A	0.34	1.38	0.132	0.0850
26b_FL citrus/ Oranges	Aerial	01-06	0.546 (0.487)	1 (1.1)	N/A	0.41	8.28	0.410	0.129

Table H.2. Dimethoate EDWCs (µg/L) for Dimethoate Uses in the U.S. Corrected for Regional PCA, Using Typical Application Rates and Numbers of Applications[1]

Scenario (bold font)/ Crops/Uses Represented	App Method	Date of First Application (DD-MM)	Aver. App Rate kg ai/A (lb ai/A)	Aver. Number of Apps	App Interval (days)	Reg. PCA	EDWCs (µg/L)[1]		
							Acute	Chronic	Cancer/ Chronic
27c_ID potatoes/ Potatoes	Aerial	20-08	0.369 (0.329)	2 (1.6)	7	0.66	5.99	0.673	**0.541**
27d_ID potatoes/ Potatoes[2]	Aerial	20-08	0.369 (0.329)	1 (1.6)[2]	N/A	0.66	3.41	0.345	0.269
28_IL corn/ Corn	Aerial	10-09	0.338 (0.302)	1 (1.1)	N/A	0.88	**10.1**	0.878	0.261
29_KS sorghum/ Sorghum	Aerial	20-08	0.298 (0.266)	1 (1.0)	N/A	0.87	4.23	0.340	0.152
30_MS soybeans/ Soybeans	Aerial	01-09	0.484 (0.432)	1 (1.0)	N/A	0.86	4.37	0.282	0.132
31_OR snap beans/ Lima beans	Aerial	01-08	0.546 (0.487)	2 (1.6)	14	0.66	2.26	0.235	0.197
32_ND wheat/ Spring wheat	Aerial	20-06	0.273 (0.244)	1 (1.0)	N/A	0.91	0.956	0.103	0.0811
33_ND wheat/ Winter wheat3	Aerial	20-06[3]	0.340 (0.303)	1 (1.0)	N/A	0.91	1.18	0.128	0.101
12b_OR Xmas trees/ Douglas fir (seed orchards) (only in OR and WA)	Airblast	01-06	1.121 (1)	1	N/A	1.0	2.10	0.220	0.206
13b_CA forestry/ Cottonwood (forest/ shelterbelt)	Aerial	01-06	1.121 (1)	1	N/A	1.0	3.97	0.452	0.470
14b_OR Xmas trees/ Hybrid cottonwood/poplar plantations (some labels allow use in ID, OR and WA)	Aerial	01-06	1.121 (1)	1	N/A	1.0	3.97	0.425	0.407
15b_CA nursery/ Citrus, non-bearing and nursery stock (only in CA and AZ)	Soil drench	01-06	1.121 (1)	1	N/A	1.0	0.450	0.0429	0.0406
17b_OR nursery/ Ornamental woody shrubs and vines; Ornamental and/or shade trees	Aerial	01-06	0.280 (0.25)	1	N/A	1.0	2.06	0.199	0.147
18b_NJ nursery/ Ornamental herbaceous plants	Soil drench	01-06	0.272 (0.243)	1	N/A	1.0	3.93	0.286	0.132

Bolded and shaded values are the highest EDWCs.

[1] Concentrations are modified using a PCA, but not using a TAF. Application rates in kg ai/ha (lb ai/A). EDWCs were rounded to three significant figures.

[2] For the ID potato scenario, one and two applications were modeled.

[3] The ND wheat scenario is set so that crop occurs in the spring; therefore, the application rate for winter spring was used, but the chemical was set to be applied during the spring instead of the winter.

[4] For the non-agricultural crops, no typical/average use information was available. EFED made certain assumptions which are described in Memo, J. Meléndez, 28-JUL-2014; D415002.