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PUBLIC COMMENTS

1. Comment from Douglas Deitch, dated 10/30/2020
2. Comment from Poison Free Malibu, dated 10/30/2020
3. Comment from Member of the Public that would like the CZ to be redrawn as a smaller area, dated 10/30/2020
4. Comment from Member of the Public wanting mention of coastal railroad issues, dated 11/2/2020
5. Comment from Beach Cities Preservation Alliance, dated 11/3/2020
6. Comment from County of Marin Board of Supervisors Dennis Rodoni, dated 11/4/2020
7. Comment from Alliance of Coastal Marin Villages, dated 11/4/2020
8. Comment from League of California Cities, dated 11/4/2020
9. Comment from Member of the Public regarding Environmental Justice, dated 11/4/2020
10. Comment from Attorney/Government Relations Consulting, dated 10/30/2020

2. Comment from Poison Free Malibu, dated 10/30/2020

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Wastewater-borne exposure of limnic fish to anticoagulant rodenticides

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ABSTRACT

The recent emergence of second-generation anticoagulant rodenticides (AR) in the aquatic environment emphasizes the relevance and impact of aquatic exposure pathways during rodent control. Pest control in municipal sewer systems of urban and suburban areas is thought to be an important emission pathway for AR to reach wastewater and municipal wastewater treatment plants (WWTP), respectively. To circumstantiate that AR will enter streams via effluent discharges and bioaccumulate in aquatic organisms despite very low predicted environmental emissions, we conducted a retrospective biological monitoring of fish tissue samples from different WWTP fish monitoring ponds exclusively fed by municipal effluents in Bavaria, Germany. At the same time, information about rodent control in associated sewer systems was collected by telephone survey to assess relationships between sewer baiting and rodenticide residues in fish. In addition, mussel and fish tissue samples from several Bavarian surface waters with different effluent impact were analyzed to evaluate the prevalence of anticoagulants in indigenous aquatic organisms.

Hepatic AR residues were detected at 12 out of 25 WWTP sampling sites in the low μg/kg range, thereof six sites with one or more second-generation AR (i.e., brodifacoum, difenacoum, bromadiolone). 14 of 18 surveyed sites confirmed sewer baiting with AR and detected hepatic residues matched the reported active ingredients used for sewer baiting at six sites. Furthermore, second-generation AR were detected in more than 80% of fish liver samples from investigated Bavarian streams. Highest total hepatic AR concentrations in these fish were 9.1 and 8.5 μg/kg wet weight, respectively and were observed at two riverine sampling sites characterized by close proximity to upstream WWTP outfalls. No anticoagulant residues were found in fish liver samples from two lakes without known influences of effluent discharges.

The findings of our study clearly show incomplete removal of anticoagulants during conventional wastewater treatment and confirm exposure of aquatic organisms via municipal effluents. Based on the demonstrated temporal and spatial coherence between sewer baiting and hepatic AR residues in effluent-exposed fish, sewer baiting in combined sewer systems contributes to the release of active ingredients into the aquatic environment.

1. Introduction

Anticoagulant rodenticides (AR) are used worldwide to control commensal rodents for hygienic and public health reasons (Buckle and Smith, 2015). Eight anticoagulants are currently approved in the European Union (EU) for biocidal use under the EU Biocidal Products Regulation No. 528/2012 (European Union, 2012), thereof three first-generation anticoagulants with maximum permissible concentrations of 0.079% (warfarin), 0.0375% (coumatetralyl), and 0.005% (chlorophacinone), and five second-generation AR with maximum permissible concentrations of 0.0075% (difenacoum), 0.005% (bromadiolone, brodifacoum, flocoumafen), and 0.0025% (difethialone) of active ingredient in bait formulations, respectively. In recent years, EU-wide application of second-generation AR has

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been increasingly restrained because of human and environmental risks and their classification as persistent, bioaccumulative, and toxic substances (Regnery et al., 2019; van den Brink et al., 2018). Until lately, however, risk mitigation measures during rodent control focused almost exclusively on the terrestrial environment (Berny et al., 2014), despite considerable acute toxicity of several AR to aquatic species. As summarized in Regnery et al. (2019), LC_{50} values (i.e., lethal AR concentration for 50% of test subjects after 96 h of exposure) for rainbow trout (*Oncorhynchus mykiss*) are in the range of 40 μg/L (brodifacoum), 51 μg/L (difethialone), 65 μg/L (difenacoum), 70 μg/L (flocoumafen), and 2860 μg/L (bromadiolone). Furthermore, brodifacoum, difethialone, and flocoumafen exhibit very high bioaccumulation potential in fish (eCA, 2016a, c, d).

The recent emergence of AR residues in the aquatic environment, amongst others their widespread occurrence in liver tissue of freshwater fish (Kotthoff et al., 2018), emphasizes the relevance and impact of aquatic exposure pathways that had previously been underestimated (Regnery et al., 2019). Several studies hypothesized that pest control in and around municipal sewer systems by local authorities and commissioned pest control professionals is one important emission source of AR in urban and suburban settings (Gómez-Canela et al., 2014a; Kotthoff et al., 2018). In Germany, the annual domestic use of AR in sewer baiting scenarios was projected as approximately 600 metric tons of bait material and 50 kg of active ingredients, respectively according to survey results from 2008 (Krüger and Solas, 2010). These quantities appear minor compared to sales volumes of common human or veterinary pharmaceuticals that are frequently detected in effluent-impacted surface waters (Ashton et al., 2004; Thomas et al., 2007). Although AR bait formulations authorized for use in sewers mainly consist of wax or fat, active ingredients are not chemically bound to the bait material and can be released upon disintegration of baits, e.g., during prolonged exposure to moist or wet conditions. From the sewers, exposure of the aquatic environment most likely occurs via wastewater treatment plant (WWTP) effluents or stormwater overflow structures in combined sewer systems that discharge highly diluted but untreated sewage directly into receiving surface waters when precipitation causes a surcharge within the system. A Spanish study reported sporadic occurrence of AR in WWTP samples in the low ng/L and μg/kg range, respectively but failed in establishing meaningful input and elimination routes (Gómez-Canela et al. 2014a, 2014b; Gómez-Canela and Lacorte, 2016). Despite shortcomings of their analytical approach (Regnery et al., 2019), results pointed toward incomplete removal of AR during activated sludge treatment and potential discharges into receiving surface waters at trace level. In laboratory tests, all AR were shown to be hydrolytically stable in water under environmentally relevant conditions and were not readily biodegradable as summarized in Regnery et al. (2019). However, a strong tendency to adsorb to organic matter combined with low water solubility and a high degree of photo-instability suggest that second-generation AR are unlikely to remain in the aqueous phase during conventional wastewater treatment. Their residues are more likely to persist and accumulate in (organic-rich) sediments, activated sludge, suspended particulate matter, and biosolids.

To date, detailed information about the fate of anticoagulants other than warfarin during conventional or advanced wastewater treatment is lacking. Moreover, multiple challenges of AR residue screening in aquatic environmental compartments were recently highlighted by Regnery et al. (2019). Notably, expected AR concentrations in WWTP effluent and receiving surface waters may be out of reach for current analytical methods and routine monitoring schemes according to worst-case predicted environmental concentrations (European Chemicals Agency, 2018; Regnery et al., 2019). Thus, we initiated a retrospective biological monitoring to assess whether trace levels of AR will occur in tertiary treated wastewater effluents and thereby cause exposure of aquatic organisms in receiving streams. We analyzed tissue samples of fish (*Cyprinus carpio*) from 25 different WWTP fish monitoring ponds in Bavaria, Germany that were provided by the Bavarian Environment Agency. These fish monitoring ponds are exclusively fed by tertiary treated municipal effluents and annually stocked with fish for six months to enable monitoring of trace level residual wastewater contaminants that might concentrate in aquatic organisms. Moreover, information about rodent control in associated sewer systems shortly before or during the respective bioaccumulation period in these fish monitoring ponds was collected by telephone survey of municipal pest control officials at selected sites in 2018 to assess potential relationships between sewer baiting and AR residues in fish. Names and exact geographic locations of WWTP sampling sites in this study are nondisclosed to preserve individual privacy of investigated WWTP and associated municipalities. To further evaluate the occurrence of anticoagulants in indigenous aquatic organisms as a function of wastewater effluent discharges, mussel and fish tissue samples from seven Bavarian streams with different degrees of municipal effluent contribution as well as two lakes without effluent discharges were also provided by the Bavarian Environment Agency and were screened for anticoagulant residues.

2. Materials and methods

Anticoagulants (i.e. eight rodenticides and two pharmaceuticals) in biological tissues were analyzed by liquid chromatography – tandem mass spectrometry (LC-MS/MS) in negative electro-spray ionization (ESI) mode after ultra-sound assisted solvent extraction and dispersive solid phase extraction (dSPE) clean-up following a QuEChERS (quick, easy, cheap, effective, rugged, and safe) approach. Fish liver samples as well as several corresponding filet samples were analyzed instead of whole-body samples because anticoagulants bind strongly to vitamin K epoxide reductase (i.e., liver is presumed to be the main organ of accumulation). Quantification of target analytes was achieved by means of individual deuterated internal standards.

2.1. Chemicals

Analytical grade standards of biocidal (i.e., warfarin, chlorophacinone, coumatetralyl, bromadiolone, difenacoum, brodifacoum, difethialone, and flocoumafen) and pharmaceutical (i.e., phenprocoumon, acenocoumarol) anticoagulants were purchased from Sigma-Aldrich (Steinheim, Germany) and Toronto Research Chemicals (TRC, North York, Ontario, Canada), respectively. Depending on availability, compound-specific deuterated analogs were used as internal standards for quantitative analysis, namely difenacoum-d4, brodifacoum-d4, flocoumafen-d4, phenprocoumon-d5 (all TRC), bromadiolone-d5, warfarin-d5, and chlorophacinone-d4 (all C/D/N Isotopes Inc., Pointe-Claire, Quebec, Canada). Difethialone-d4 was custom-synthesized (TLC, Aurora, Ontario, Canada), but delivery was delayed until completion of analyses. Stock solutions of individual compounds were prepared in methanol and aliquots were taken to compose respective mixtures of natives and isotopes at the 200 ng/mL level in methanol. Organic solvents and ultrapure water used for preparation of solutions, extraction, and chromatography were HPLC grade. Reagents utilized for sample preparation were analytical grade except magnesium sulfate and sodium chloride (reagent grade, Agilent Technologies, Waldbronn, Germany).

2.2. Sampling sites and handling of samples

All biological tissue samples analyzed in this study were kindly provided by the Bavarian Environment Agency. Sample material from the Bavarian Specimen Bank (frozen at −20 °C, homogenized, wrapped in aluminum foil and vacuum-sealed) was shipped overnight on dry-ice to the Federal Institute of Hydrology laboratory to ensure an uninterrupted cool chain. Parameters such as species, total length, total weight, organ weight, age, gender, Fulton's condition factor (CF), hepatosomatic index (HSI), and gonadosomatic index were made available for each fish sample.

Bavarian state regulation requires the operation of ponds for an active fish monitoring (herein after referred to as bioaccumulation ponds) by municipal WWTP with equal to or more than 100,000 person equivalents. The majority of these WWTP facilities employ conventional treatment (i.e., mechanical, biological, chemical). The surface area size of bioaccumulation ponds is mostly in the range of 20–130 m^2 with an average depth of 1 m and a hydraulic retention time of more than 3 d (Bayerisches Landesamt für Umwelt, 2012a). They are exclusively fed by municipal effluents and annually stocked with 10 carp (*C. carpio*) (i.e., individuals of the same age and bloodline from the fish rearing ponds at the Bavarian Environment Agency) for a six months exposure period to enable active monitoring of potential adverse effects and bioaccumulation of residual contaminants (Bayerisches Landesamt für Umwelt, 2012b). All of the stocked carp are self-feeding and not allowed to be fed throughout the bioaccumulation period to prevent contamination and bias.

Of the active monitoring in 2015 (bioaccumulation period April through October), 31 liver and 12 corresponding filet samples of individual carp were received from 25 different WWTP bioaccumulation ponds (herein referred to as WWTP A – WWTP Y) for analysis in 2017 and 2018. Tissue samples of three individuals from the same bioaccumulation pond were analyzed as replicates at three sites (WWTP A, WWTP B, and WWTP C). At site WWTP C, one liver sample of the 2014 bioaccumulation period was also investigated. Moreover, one wastewater unexposed carp liver sample was obtained from the Bavarian Environment Agency's fish rearing ponds as a reference. Pooled zebra mussel samples (*Dreissena polymorpha*, n = 2) and individual fish liver (n = 14) and filet (n = 3) samples of chub (*Squalius cephalus*), perch (*Perca fluviatilis*), and pike (*Esox lucius*) had been collected from seven Bavarian streams (i.e., Amper, Danube, Iller, Isar, Lech, Main, Vils) and two lakes (i.e., Starnberger See, Weißensee) in 2013–2016 as part of the EU Water Framework Directive 2000/60/EC monitoring program. Detailed information about all samples is provided in the supplementary material (SM, Tables S1 and S2). Though not necessarily in close proximity to WWTP outfalls, the riverine sampling sites were situated upstream and downstream of several WWTP that were part of the active biological WWTP monitoring. A general map highlighting all surface water sampling sites can be found in the SM (Fig. S1).

2.3. Determination of total lipids in biological tissue samples

Total lipid content in homogenized tissue samples was determined according to Smedes (1999). A detailed description is provided in the SM. Percent lipid for each sample was determined by dividing the lipid weight for each sample by the initial wet weight of each individual sample.

2.4. Sample extraction and clean-up

The chosen QuEChERS approach followed general procedures described by Vudathala et al. (2010) and Morrison et al. (2016). Approximately 1–2 g wet weight of homogenized fish liver or filet sample was suspended in 3.2 mL acetonitrile and 0.8 mL acetone acidified with 0.1% formic acid (v/v) in a 50 mL polypropylene centrifuge tube using a vortex shaker (MS2 Minishaker, IKA). For extraction of pooled soft body mussel samples, approximately 0.3 g of freeze-dried material was used. Internal standard mix (25 μL of 200 ng/mL each in methanol) as well as 0.2 g magnesium sulfate and 0.2 g sodium chloride salts (Agilent Technologies) were added to the sample tube. The tube was capped tightly and immediately vortexed for 60 s. Following 30 min in an ultra-sonication bath at 20 °C, 4 mL of fresh acidified acetone was added to the sample and the extraction step was repeated. Subsequently, sample tubes were stored in a freezer at −20 °C overnight to enhance protein precipitation. Afterwards, samples were centrifuged for 5 min at 2000 rcf (relative centrifugal force) and the crude extract was transferred to a 15 mL polypropylene centrifuge tube for further clean-up via dSPE. dSPE facilitated removal of co-extracted compounds (e.g., phospholipids) and helped reduce matrix interferences during LC-MS/MS analysis. The amount of applied dSPE bulk sorbents varied depending on tissue type. dSPE of liver extracts was carried out using 0.3 g magnesium sulfate together with 0.1 g each of primary-secondary amine bonded silica, end-capped C_{18} material, florisil (60–100 mesh), and basic alumina. Clean-up of filet or mussel extracts required less sorbents (i.e., half the amount used for liver tissue). Prior use, florisil and basic alumina had been activated in an oven at 350 °C for 12 h followed by the addition of 2% (v/w) ultrapure water. The dSPE tubes were tightly capped and immediately vortexed for 60 s. After 5 min rest, samples were centrifuged. The organic phase was retrieved, evaporated to dryness under nitrogen, and resolved in 500 μL methanol. A 200 μL subsample thereof was diluted with ultrapure water at a ratio of 1:1 (v/v) and transferred to a Thomson Single Step filter vial (PTFE membrane, 0.45 μm pore size) for LC-MS/MS analysis.

Aliquots of pooled homogenized residue-free fish livers (n = 6), filets (n = 3), and freeze-dried mussel soft bodies (n = 4) were fortified with target substances at low concentration (i.e., 1–2 g of wet fish tissue or 0.3 g of freeze-dried mussel tissue spiked with 25 μL of 200 ng/mL standard mix) and were analyzed to validate the optimized extraction and clean-up procedure. Mean recoveries and standard deviations for each analyte are provided in Table S3, SM. Besides residue-free reference tissues (procedural blanks), each batch of samples included a low-level fortified matrix control that was processed in the same way as samples. To prevent cross-contamination of samples, all glass ware was rinsed with acetone prior cleaning in the dishwasher and heated at 350 °C for several hours afterwards. Polypropylene centrifuge tubes were only used once and were discarded after extraction and clean-up.

2.5. Analysis of anticoagulants by LC-MS/MS

LC-MS/MS analysis was performed on an Agilent 1260 Infinity LC system equipped with a high-precision liquid autosampler and temperature-controlled column compartment (40 °C) coupled with a Sciex 4500 QTrap MS/MS system. The sample injection volume was 10 μL. Prior injection, a 20 s needle wash with isopropanol was performed at the flush port to minimize sample carry-over. A binary gradient at a flow rate of 0.6 mL/min was used to separate compounds on a Phenomenex 50 × 2 mm Luna PFP column with 3 μm particle size and upstream security guard cartridge. Chromatographic separation of individual AR stereoisomers was not intended. Eluents consisted of (A) 4 mM ammonium acetate solution in water and (B) methanol with the following gradient: 20% B held for 0.5 min, stepped to 90% at 3.5 min, then held at 90% B for 0.5 min before returning to 20% B at 4.5 min. A 2.5 min equilibration step at 20% B resulted in a total run time of 7 min. Two mass

transitions (i.e., quantifier and qualifier) were monitored for each analyte in ESI negative mode using scheduled multiple reaction monitoring. The monitoring window for each transition was 60 s with a target scan time of 1 s. Monitored mass transitions and compound specific tuning parameters are summarized in Table S4, SM.

Qualitative and quantitative analyses were performed in Analyst (version 1.6.3) and MultiQuant (version 3.0). An internal standard calibration was used for quantification. Eight calibration standards over the concentration range of 0.01−5 ng/mL were analyzed within each LC-MS/MS sequence run. Analytes without isotope-labeled analogs were quantified based on bromadiolone-d5 (difethialone) and warfarin-d5 (coumatetralyl, acenocoumarol). Analyte peaks with a signal-to-noise ratio of less than 10 or 3 of the mass transitions used for quantification and confirmation, respectively or shifted retention time compared to their respective isotope-labeled analogs were discarded from further data evaluation. All reported analyte concentrations in biological tissues are based on wet weight and account for analyte loss and ion suppression during sample extraction, clean-up, and LC-MS/MS analysis. Accuracy and precision of the method was checked within each measurement series by repeated injections of reference samples (i.e., procedural blanks, low-level fortified matrix controls). Method detection limits for all analytes in tissue materials ranged between 0.01 μg/kg and 0.3 μg/kg wet weight.

2.6. Sewer baiting survey at selected sites

Operators and administrators in charge of municipal pest control at 11 WWTP sampling sites with evidence of AR residues were surveyed in May 2018 to retrospectively obtain information about rodent control in associated sewer systems shortly before or during the 2015 bioaccumulation period of carp in respective bioaccumulation ponds. Furthermore, 7 WWTP samplings sites without evidence of AR residues in fish were contacted. Surveyed information covered relevant WWTP operational parameters, sewer system specifics, applied pest control schemes within municipal purview (i.e., mechanical or chemical, frequency, duration, types of active ingredients, bait amount and placement), as well as other known (or assumed) sources of AR in the catchment area. The narrow selection of surveyed sites as well as variable quality of mined data allowed for qualitative but not quantitative statistical analysis of survey results.

3. Results and discussion

3.1. Residues of anticoagulants in fish from wastewater treatment plant bioaccumulation ponds

Although effluent-dominated systems such as bioaccumulation ponds represent worst-case exposure scenarios for fish, they provide valuable insight regarding the bioaccumulation potential of effluent-sourced contaminants in indigenous aquatic organisms. At 12 out of 25 studied sampling sites, AR residues were detected in the livers of individual carp in the low μg/kg range after being exposed to municipal effluents for approximately six months. No distinct correlation between AR concentration in fish and WWTP treatment capacity (i.e., population equivalents) was observed (Fig. 1). A total of six sites revealed hepatic residues of one or more second-generation AR. Due to the high frequency of non-detect data (i.e., less-than values) throughout the samples, analyte detection frequencies, median, 95th percentile, and maximum concentrations are listed in Table 1. Average biometric parameters of the analyzed two-year old carp (14 male, 8 female, 10 undetermined) were 35.7 ± 3.7 cm total length, 769 ± 258 g whole-body weight, and 6.2 ± 3.3% lipid content in liver tissue (Table S2, SM).

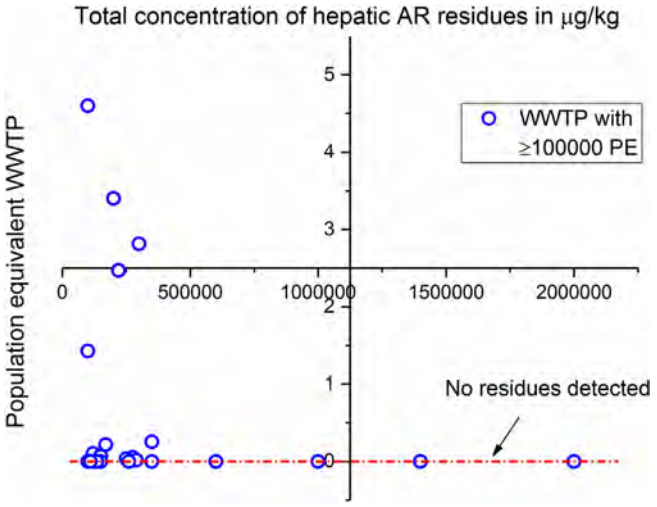

Fig. 1. Detected total concentration of anticoagulant rodenticides (AR) in carp liver samples from 25 Bavarian municipal wastewater treatment plant (WWTP) bioaccumulation ponds with treatment capacities between 100,000 and 2,000,000 population equivalents (PE).

Interestingly, the first-generation AR coumatetralyl was detected most frequently in carp from bioaccumulation ponds (Table 1). It was followed by the second-generation AR bromadiolone, brodifacoum, and difenacoum, all of which had higher detection limits than coumatetralyl (Table 1). Notably, multiple individuals from the same sampling site had matching distributions and comparable concentrations as shown for treatment facilities WWTP A, B, and C (Tables 2 and S2, SM), pointing towards identical exposure of fish individuals via nondietary and/or dietary routes. In contrast, difethialone was solely observed in one liver sample at WWTP B, which was more likely due to individual dietary uptake rather than nondietary routes. Few studies hypothesized that terrestrial invertebrates feeding on AR containing bait may function as vector in the environment (Masuda et al., 2014; Pitt et al., 2015). No residues of flocoumafen and chlorophacinone were detected in any of the analyzed samples from the bioaccumulation ponds (Tables 1 and 2) and no anticoagulant residues were detected in carp liver of a wastewater unexposed sibling that had been analyzed as a reference (Table S2, SM). With the exemption of coumatetralyl, none of the analyzed corresponding filet samples (on average 0.9 ± 0.5% lipid content) contained anticoagulant residues (Table 2). At WWTP C traces of coumatetralyl were observed in filet samples of all three individuals. The coumatetralyl residues in filet tissue were an indication for ongoing exposure at the time of sampling as active ingredient not yet bound to protein (e.g., in the liver or blood plasma) is expected to quickly depurate in fish based on laboratory bioconcentration studies (eCA, 2016b). In good agreement, corresponding liver samples revealed substantial coumatetralyl residues (Table 2). WWTP C also exhibited highest hepatic concentration of total AR in a single organism (4.6 μg/kg, Fig. 1). In comparison, lower hepatic concentrations of total AR (1.1 μg/kg) and fewer active ingredients were detected during the 2014 bioaccumulation period at site WWTP C. While residues of difenacoum (1.0 μg/kg), bromadiolone (0.1 μg/kg) as well as phenprocoumon (0.36 μg/kg) were in the range of concentrations observed in liver samples of the 2015 bioaccumulation period (Table 2), no other AR residues were present. This implies that even at the same site wastewater-borne rodenticide emissions will vary over consecutive years due to variable usage patterns and multiple emission sources. Differences in the diversity of AR residues over time was recently reported by

Table 1
Analyte detection frequencies, median, 95th percentile, and maximum concentrations of anticoagulants in fish liver samples from different municipal wastewater treatment plant bioaccumulation ponds and nearby receiving streams. Analyte concentrations are reported in μg/kg relating to wet weight. ND = not detected; '<' denotes values below the respective method detection limit.

Analyte	Liver tissues from 25 bioaccumulation ponds [a], n = 32				Liver tissues from 7 receiving streams, n = 12			
	Frequency	Median	95th percentile	Maximum	Frequency	Median	95th percentile	Maximum
	(%)	(μg/kg)	(μg/kg)	(μg/kg)	(%)	(μg/kg)	(μg/kg)	(μg/kg)
Rodenticides								
Brodifacoum	34.4	<0.3	1.6	1.9	66.7	1.7	5.4	6.4
Bromadiolone	37.5	<0.1	1.0	2.0	41.7	<0.1	1.2	2.0
Difenacoum	28.1	<0.3	1.6	1.8	25.0	<0.3	1.2	1.8
Flocoumafen	ND	ND	ND	ND	25.0	<0.01	0.6	1.0
Difethialone	3.1	<0.1	<0.1	0.8	25.0	<0.1	2.7	5.2
Chlorophacinone	ND	ND	ND	ND	16.7	<0.1	0.4	0.6
Coumatetralyl	40.6	<0.01	1.1	1.6	8.3	<0.01	0.01	0.02
Warfarin	9.4	<0.01	0.04	0.05	ND	ND	ND	ND
Σ Rodenticides [b]	59.4	0.06	4.0	4.6	83.3	2.6	8.8	9.1
Pharmaceuticals								
Phenprocoumon	76.9 [c]	0.3	1.0	1.8	83.3	0.04	0.1	0.2
Acenocoumarol	5.3 [c]	<0.01	0.01	0.01	ND	ND	ND	ND

[a] At three sites with hepatic anticoagulant rodenticide residues, multiple individuals (n = 3) of the same bioaccumulation pond were analyzed.
[b] At least one of 8 anticoagulant rodenticides detected.
[c] Limited number of samples analyzed (n = 26).

Table 2
Occurrence of anticoagulants in corresponding liver and filet samples of multiple individuals from select municipal wastewater treatment plant (WWTP) sampling sites in Bavaria, Germany in 2015. Mean analyte concentrations and standard deviations (SD) are reported in μg/kg relating to wet weight. ND = not detected.

Analyte	WWTP A		WWTP B		WWTP C	
	Liver (n = 3)	Filet (n = 3)	Liver (n = 3)	Filet (n = 3)	Liver (n = 3)	Filet (n = 3)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
	(μg/kg)	(μg/kg)	(μg/kg)	(μg/kg)	(μg/kg)	(μg/kg)
Rodenticides						
Brodifacoum	1.5 ± 0.1	ND	0.8 ± 0.1	ND	1.3 ± 0.6	ND
Bromadiolone	1.3 ± 0.6	ND	0.4 ± 0.1	ND	0.2 ± 0.0	ND
Difenacoum	ND	ND	1.5 ± 0.2	ND	1.3 ± 0.5	ND
Flocoumafen	ND	ND	ND	ND	ND	ND
Difethialone	ND	ND	0.3 ± 0.4	ND	ND	ND
Chlorophacinone	ND	ND	ND	ND	ND	ND
Coumatetralyl	ND	ND	0.1 ± 0.1	ND	1.3 ± 0.3	0.02 ± 0.00
Warfarin	ND	ND	ND	ND	ND	ND
Σ Rodenticides [a]	2.9 ± 0.5	ND	3.0 ± 0.5	ND	4.1 ± 0.7	0.02 ± 0.00
Pharmaceuticals						
Phenprocoumon	0.3 ± 0.1	ND	0.3 ± 0.1	ND	0.2 ± 0.1	ND
Acenocoumarol	0.01 ± 0.00	ND	ND	ND	ND	ND

[a] Sum of detected anticoagulant rodenticides per individual.

Kotthoff et al. (2018) for two riverine sampling sites based on decennial temporal trend analysis of fish liver samples that were obtained from the German Specimen Bank.

The presence of warfarin in wastewater has mainly been linked to the consumption of blood-thinning medication by resident population as warfarin is the only biocidal anticoagulant that is concurrently authorized for pharmaceutical use (Ajo et al., 2018; Regnery et al., 2019; Santos et al., 2013). To date, the 4-hydroxycoumarin derivatives phenprocoumon and acenocoumarol are primarily used across continental Europe instead of warfarin to prevent and treat thromboembolic diseases besides direct coagulation factor inhibitor drugs (Fan et al., 2018; Lin et al., 2013). Medical consumption of phenprocoumon exceeds that of warfarin by approximately factor 40 according to German prescription statistics (Regnery et al., 2019). Congruently, hepatic residues of phenprocoumon were detected in 76.9% of carp from bioaccumulation ponds with a maximum level of 1.8 μg/kg whereas hepatic warfarin residues were only observed at trace level in less than 10% of samples with a maximum of 0.05 μg/kg (Table 1). The more pronounced hepatic phenprocoumon residues in effluent-exposed fish can be explained by the higher frequency and amplitude of contaminant loading considering that both substances are extensively metabolized in the human body. Only about 2% of the typical daily warfarin prescription dose is excreted as unchanged active ingredient (Crouse et al., 2012; Park, 1988). Phenprocoumon is excreted almost entirely as a glucuronide conjugate, with less than 10% of the dose as unchanged drug (Kasprzyk-Hordern, 2010).

Data summarized in Table 1, Fig. 1, and Table S5 corroborate the assumption that AR input rates are of transient character and will fluctuate depending on site-specific factors such as usage patterns and runoff regimes in urban and suburban catchments, hydrometeorological conditions, and WWTP operational parameters and performance. All of the investigated municipal WWTP in this study applied tertiary treatment, i.e., each treatment train consisted of mechanical treatment followed by biological treatment stages

and chemical dosing for enhanced nutrient removal. Treatment capacities varied between 100,000 and 2,000,000 population equivalents (Bayerisches Landesamt für Umwelt, 2012b) with average daily dry weather effluent discharges in the range of 5000 to 570,240 m^3/d (Table S5, SM). Yet, discharges could quadruplicate during wet weather at facilities with mainly combined sewer systems connected (majority of investigated sites). None of the treatment facilities with confirmed second-generation AR residues in fish (WWTP A – F, Table S5, SM) applied further advanced treatment. Downstream advanced treatment stages that are focused on elimination of refractory wastewater-borne trace organic chemicals, such as ozone, advanced oxidation processes, membrane filtration, or activated carbon filtration, are still not common at full-scale facilities in Germany (Schaar and Kreuzinger, 2017). Nevertheless, several neighboring WWTP sites discharging into the same stream (i.e., along the upper and middle stretch of Isar River) operate downstream biological active sand filters (Table S5, SM). Although some of these facilities also run ultra-violet (UV) disinfection units during bathing season to meet microbial bathing water quality requirements, effluents feeding the bioaccumulation ponds had been diverted prior to disinfection according to personal communication with WWTP operators. While no second-generation AR residues were detected in fish samples from sampling sites with further advanced treatment (e.g., WWTP N, O, R, and S), low levels of hepatic phenprocoumon residues were frequently observed, indicating incomplete retention of this hydroxycoumarin derivative in biological active sand filters. Given their aforementioned physicochemical properties (e.g., not readily biodegradable, low water solubility, high lipophilicity, and photolytic instability) at ambient environmental conditions, second-generation AR might occur particle-bound in wastewater effluents rather than freely dissolved, although a previous study implied enhanced solubility or co-solubility of second-generation AR in organic-rich water (Pitt et al., 2015). Depending on the treatment train of investigated facilities, remaining suspended particle loads in the discharged effluents were generally in the range of 2–10 mg/L under dry weather conditions (Table S5, SM).

A previous investigation observed no relationship between fish length, total weight, and WWTP treatment capacity, whereas factors such as pond size and type were identified as major driver for fish condition in the bioaccumulation ponds (Bayerisches Landesamt für Umwelt, 2012b). Yet, site-specific distributions of AR were further evaluated based on available physiological fish health parameters (e.g., length, weight, lipid content, organ weight) and are shown as a function of Fulton's CF and HSI in Fig. 2. Overall, occurrence and distribution of AR residues expressed no distinct relationship with gender, lipid content, and physiological parameters of fish health such as CF or HSI. Fulton's CF for carp should generally be higher than 1 to indicate adequate nutritional state. Values for CF and HSI were on average 1.6 ± 0.2 and 2.8 ± 0.8, respectively (Table S2, SM). Teubner et al. (2015) concluded earlier that Fulton's CF and HSI might be no meaningful stress indicators. Nevertheless, adverse effects of chronic AR exposure in fish from these bioaccumulation ponds could have been masked by other stressors or influential factors that we were not able to account for in retrospect at the investigated 25 WWTP.

In summary, our results provide crucial evidence that anticoagulants are not completely removed during conventional biological wastewater treatment and thus confirm one important exposure pathway for indigenous aquatic organisms: anticoagulants will enter the aquatic environment by way of effluent discharges. Furthermore, these findings also show that second-generation AR can bioaccumulate in fish liver under environmentally realistic conditions and exposure scenarios.

3.2. Potential sources of anticoagulant rodenticides in wastewater

Considering anticoagulants' high protein binding capacity and the persistence of specifically second-generation AR in liver tissues of terrestrial wildlife (Horak et al., 2018), it is difficult to link hepatic AR residues in fish to distinct exposure events. Besides the aforementioned release of pharmaceutical anticoagulants (e.g., phenprocoumon, warfarin) due to medical consumption, pest control in

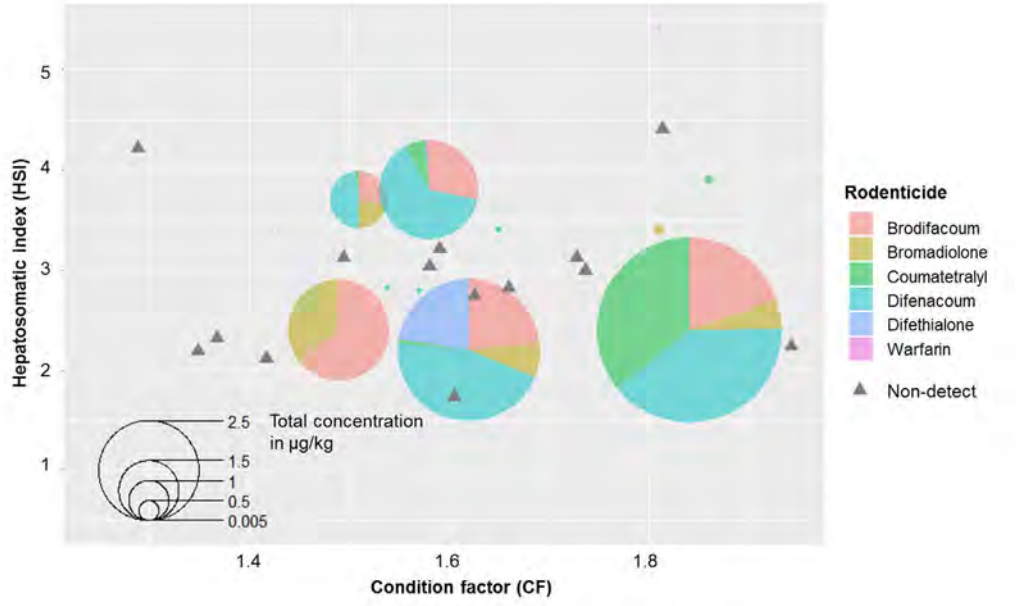

Fig. 2. Anticoagulant rodenticide residues in fish liver samples (n = 25) from 25 different municipal wastewater treatment plant bioaccumulation ponds (i.e., two-year-old carp after 100% wastewater effluent exposure for 6 months) and one wastewater unexposed reference liver plotted as a function of Fulton's condition factor (CF) and hepatosomatic index (HSI). Analyte concentrations are reported in µg/kg relating to wet weight.

and around municipal sewer systems in urban and suburban settings is assumed to be the major emission source of AR into wastewater. Notably, 78% of operators and administrators at the 18 surveyed sampling sites confirmed sewer baiting with AR, whereas 17% negated pest control enforcement in their sewers in 2015 (Table S5, SM). One municipality used a mechanical rat trap system. Based on available information, mainly bait blocks were used when baiting with AR. In general baits were attached to the manhole's gully trap or step irons by wire to prevent dragging off or flushing away. At most surveyed sites, however, deployed baits remained in the sewers after baiting campaigns ended and were not removed for disposal. Individual annual quantities deployed in the sewers ranged between 500 and 2500 baits (mostly 200 g bait blocks) among the 11 municipalities that provided quantitative information (Table S5, SM). This corresponded to a total of approximately 3000 kg of bait material per 2,500,000 person equivalents. At all surveyed sites, products containing difenacoum, warfarin, bromadiolone, or brodifacoum were exclusively used (Table S5, SM). Oftentimes multiple products with different active ingredients were applied over the course of one control measure. Based on provided information by municipal pest control officials, detected AR residues in fish liver matched the reported active ingredients used for sewer baiting at six sampling sites (Fig. 3), namely at WWTP A, B, D, E, I, and K (Table S5, SM). Interestingly, traces of warfarin residues in carp from WWTP D, I, and K concurred with confirmed deployment of warfarin baits during sewer baiting in the associated sewer systems.

Despite the demonstrated temporal and spatial coherence, evidence of specific emission sources and pathways remains challenging considering their wide application range. While existing data suggest that pest control professionals are among the main users of biocidal AR in Germany, agribusinesses, local authorities, and household consumers represent other important user groups (Regnery et al., 2019). For instance, the second-generation AR detected in fish liver at WWTP F did not match the second-generation AR supposedly used for sewer baiting by its largest connected municipality (Fig. 3 and Table S5, SM). It became apparent that WWTP F received wastewater from 11 additional communities, which were not part of the survey. Thus, the proportional dry weather discharge of the surveyed municipality was only in the range of approximately 30%. Moreover, at least four surveyed sites with confirmed second-generation AR sewer baiting in 2015 revealed no corresponding residues in fish. At two sites thereof (i.e., WWTP G and J), municipal pest control officials reported that untouched bait blocks had been removed from the sewers for appropriate disposal at the end of their baiting campaigns. In both samples solely traces of hepatic coumatetralyl residues were found. In Germany, none of the registered products containing coumatetralyl are permitted for use in sewer baiting scenarios. However, the use of first-generation AR such as coumatetralyl is less restricted. Information provided by German stakeholder groups and a recent study by Koivisto et al. (2018) suggest that coumatetralyl is more frequently used by agribusinesses and private consumers rather than pest control professionals or municipalities.

It can be concluded that sewer baiting contributes to the release of active ingredients into wastewater. Baits deployed in combined sewer systems and stormwater channels face a substantial risk of prolonged exposure to moist or wet conditions and thus scouring when precipitation causes a sudden surcharge within the system due to frequently occurring extreme weather events such as torrential downpours in urban and suburban areas. This is even more critical for the application of AR containing baits in stormwater channels that are not connected to retention basins or WWTP but discharge directly into natural water bodies. Nonetheless, the risk of active ingredient release during chemical pest control measures in sewer systems can be minimized if contact of bait material with water and wastewater is strictly excluded (e.g., by use of devices that keep the bait dry, deployment of baits exclusively in manholes free from backing-up/runoff pouring in, collection and appropriate disposal of remaining bait at the end of baiting campaigns).

Besides sewer baiting, additional emission sources of AR into sewer systems and WWTP are surmised and require further investigation. Potential other emission scenarios include baits or poisoned carcasses being flushed into the sewers during outdoor surface baiting (e.g., near storage facilities for goods or food production, public green space, private or communal garden plots), incorrect disposal of baits, landfill leachate, recirculate from sludge dewatering processes, or washing of disposed organic material containing active ingredients prior incineration. Deployment of baits in the immediate vicinity of watercourses represents another

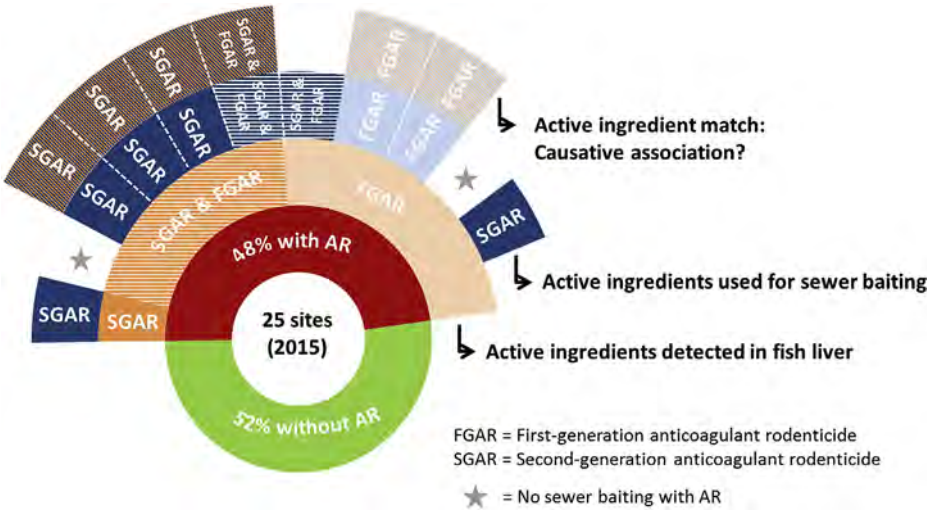

Fig. 3. Potential relationship between detected anticoagulant rodenticide (AR) liver residues in carp from select effluent-fed wastewater treatment plant bioaccumulation ponds and AR bait application in associated sewer systems during rodent control based on survey results. Only survey results for sampling sites with AR residue evidence are shown. One site with detected first-generation AR residue declined to participate in the survey.

likely emission source of AR into the aquatic environment, e.g., due to wash off from bank slopes, aboveground bait stations, or rodent burrows, respectively as well as contaminated run-off (European Chemicals Agency, 2018). Although mandatory instructions for use and risk mitigation measures were stipulated at EU-level and best practice guidelines were established during national product authorizations to minimize the risks of environmental exposure (Umweltbundesamt, 2019), the extent of compliance with these provisions and guidelines is largely unknown. Previous studies assumed that the typical use of AR commonly violates respective use and disposal instructions (Koivisto et al., 2016). It should be noted that anticoagulants are currently not approved as active ingredients in plant protection products in Germany. Operators at WWTP C confirmed that no sewer baiting with AR had been conducted in their associated combined sewer system over the past 10 years (Table S5, SM). Yet, WWTP C was the site with the highest number and total concentration of AR residues (i.e., brodifacoum, bromadiolone, difenacoum, and coumatetralyl) among the 2015 carp liver samples. Furthermore, bromadiolone and difenacoum were also detected in carp liver from the same site in 2014 as discussed earlier.

3.3. Occurrence and fate of anticoagulants in fish and mussels from lakes and receiving streams

Prolonged input rates of anticoagulants from effluent loadings, even at trace level, can increase the effective exposure duration of organisms residing in receiving aquatic systems if input rates exceed environmental dissipation rates. In most upper river basins in Germany, wastewater effluent contributions during average flow conditions vary between 0 and 5% according to a recent study by Karakurt et al. (2019). Contributions of more than 5–10% and more than 10–20%, respectively are prevalent in river basins up- and downstream of urban centers as well as river stretches generally characterized by low-flow conditions (e.g., Main River). During low-flow conditions, however, effluent contributions of more than 10–20% are common for a large number of river basins nationwide, whereas several water-sheds exhibit wastewater effluent contributions of more than 20–30% (Karakurt et al., 2019).

As expected based on available information about their environmental fate and minor medical consumption in Germany, warfarin and acenocoumarol were not detected in any of the biological tissue samples from wild freshwater fish (Table 1). While phenprocoumon traces were detected in 83.3% of fish samples from receiving streams, its median concentration in liver tissue was only 0.04 μg/kg with a maximum of 0.2 μg/kg (Table 1), corroborating marginal bioaccumulation potential in indigenous aquatic organisms. In contrast, a 40-fold higher median concentration of brodifacoum was observed in these liver tissue samples. Overall, residues of second-generation AR were detected in more than 80% of fish liver samples (mainly chub, 4–11 years) from investigated Bavarian streams with different degrees of municipal effluent contributions (Fig. 4). Residues were detected in individuals from Amper (n = 1, approx. 0–5% wastewater effluent contribution during average flow conditions at this sampling site), Iller (n = 1, approx. 0–5%), Isar (n = 2, approx. 5–10% at both sites), Lech (n = 1, approx. 0–5%), and Main (n = 5, approx. 9–11% throughout sites), whereas no residues were observed in two individuals from sampling sites at Danube (approx. 5–10%) and Vils (approx. 0–5%), respectively. As summarized in Table 1, brodifacoum (66.7%) was most frequently detected followed by bromadiolone (41.7%), difenacoum (25%), flocoumafen (25%), and difethialone (25%). The high detection frequency of hepatic brodifacoum residues in our study concurs with findings by Kotthoff et al. (2018) in 8–12 year old limnic bream. Likewise, no anticoagulant residues were found in liver samples of pike from two lakes (i.e., Starnberger See and

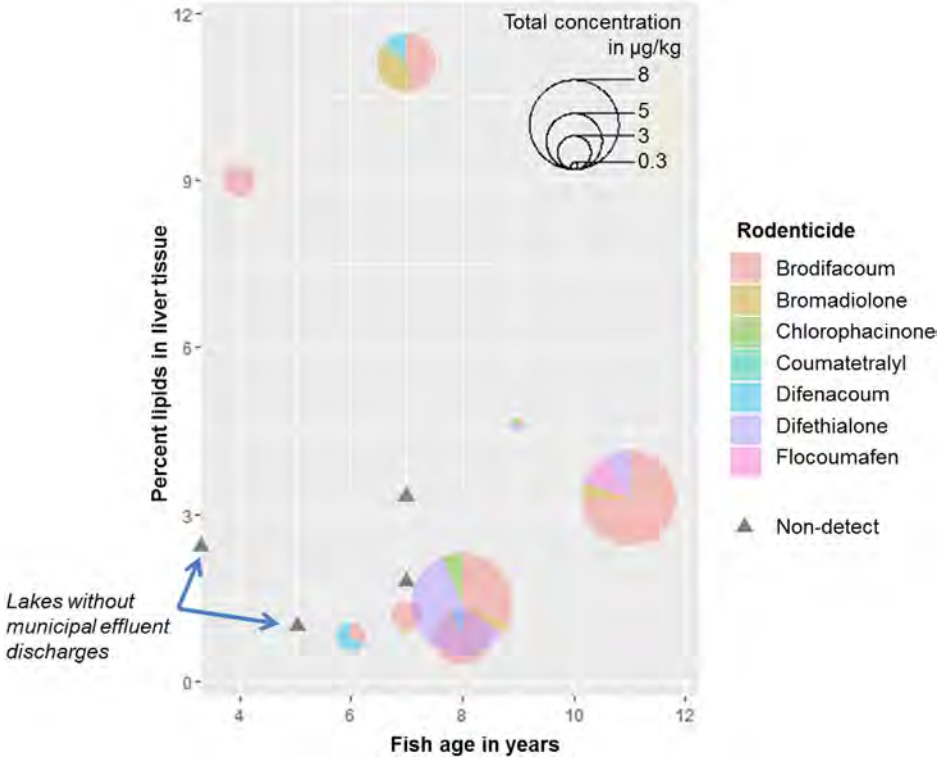

Fig. 4. Measured concentration of anticoagulant rodenticides in 14 fish liver samples (i.e., chub, pike, perch) from 9 different surface waters (i.e., two lakes and 7 streams) in Bavaria, Germany. Analyte concentrations are reported in μg/kg relating to wet weight.

Weißensee) without known influences of effluent discharges (Fig. 4).

The highest total AR concentrations were in the range of 9.1 and 8.5 μg/kg and were observed in an 8-year old chub from the lower stretch of Isar near its confluence with Danube and an 11-year old from Main near Rothwind (Fig. 4 and Table S1). Both sampling sites are characterized by close proximity to upstream WWTP outfalls according to their technical data sheets (accessed on 01/18/19 at https://www.gkd.bayern.de/de/fluesse/biologie/). In a 9-year old individual from a second sampling site at the middle stretch of Isar near Moosburg (Table S1 and Fig. S1, SM), solely traces of hepatic flocoumafen residue (0.1 μg/kg) were detected. This sampling site is situated downstream of several WWTP sampling site outfalls with non-detects of AR in effluent-exposed carp as discussed in section 3.1. At Main River, all five individuals from four different sampling sites along its upper and middle stretch (Table S1 and Fig. S1, SM) revealed hepatic residues of at least one second-generation AR. Their total AR concentrations ranged between 1.3 and 8.5 μg/kg (Fig. 4). It was estimated that portions of Main receive effluent contributions of more than 30–50% under low water conditions (Karakurt et al., 2019). Analyzed corresponding filet samples of three individuals from Main River revealed no residues (Table S1, SM). Interestingly, no AR residues were detected above their respective method detection limits in pooled mussel samples from two Main sampling sites, thereof one site with confirmed hepatic AR residues in fish (Fig. S1 and Table S1, SM). As reported in previous studies, bioaccumulation processes can widely differ among aquatic species due to complex interactions between various routes of uptake, excretion, passive release, and metabolization (Streit, 1998). Furthermore, substantial data gaps exist regarding the understanding of exposure pathways and potential adverse effects of chronic exposure with multiple active ingredients (Rattner et al., 2014), making it nearly impossible at the moment to estimate the consequences of chronic AR exposure to freshwater fish. Nonetheless, very persistent second-generation AR such as brodifacoum will likely accumulate in the aquatic food chain when released into the aquatic environment and put predators at risk (Ruiz-Suarez et al., 2016; Serieys et al., 2019).

4. Conclusions

Our results clearly indicate incomplete removal of AR during conventional wastewater treatment and confirm indirect exposure of aquatic organisms via WWTP effluents. Our findings also confirm high hepatic bioaccumulation potential and persistence of second-generation AR in indigenous limnic fish. Based on the demonstrated temporal and spatial coherence between sewer baiting and hepatic anticoagulant residues in effluent-exposed fish, sewer baiting in combined sewer systems contributes to the release of active ingredients into raw wastewater and receiving streams, respectively. Nevertheless, realistic exposure estimations for the aquatic environment remain challenging given the non-disclosure or non-existence of domestic market data on rodenticide sales, use, and disposal. Future research should focus on identifying the ecotoxicological consequences of chronic rodenticide exposure to indigenous freshwater fish at concentrations relevant for surface water bodies. As for most terrestrial species, a link between hepatic AR residue levels in fish and species-specific lethal or sub-lethal effect concentrations and their population relevance is still missing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.watres.2019.115090.

References

Ajo, P., Preis, S., Vornamo, T., Mänttäri, M., Kallioinen, M., Louhi-Kultanen, M., 2018. Hospital wastewater treatment with pilot-scale pulsed corona discharge for removal of pharmaceutical residues. J Environ Chem Eng 6 (2), 1569–1577.
Ashton, D., Hilton, M., Thomas, K.V., 2004. Investigating the environmental transport of human pharmaceuticals to streams in the United Kingdom. Sci. Total Environ. 333 (1–3), 167–184.
Bayerisches Landesamt für Umwelt, 2012a. Bioakkumulation bei Abwasseranlagen für biologisch abbaubares Abwasser - Merkblatt Nr. 4.7/4. Bayerisches Landesamt für Umwelt, Augsburg, Germany, p. 13 (in German).
Bayerisches Landesamt für Umwelt, 2012b. Bioakkumulation bei bayerischen Kläranlagen - Ergebnisse von 2003 bis 2009 (anonymisiert). Bayerisches Landesamt für Umwelt, Augsburg, Germany, p. 20 (in German).
Berny, P., Esther, A., Jacob, J., Prescott, C., 2014. Risk Mitigation Measures for Anticoagulant Rodenticides. European Commission, Luxembourg, p. 104.
Buckle, A.P., Smith, R.H. (Eds.), 2015. Rodent Pests and Their Control. CAB International, Wallingford, UK.
Crouse, B.A., Ghoshdastidar, A.J., Tong, A.Z., 2012. The presence of acidic and neutral drugs in treated sewage effluents and receiving waters in the Cornwallis and Annapolis River watersheds and the Mill CoveSewage Treatment Plant in Nova Scotia, Canada. Environ. Res. 112, 92–99.
eCA, 2016a. Brodifacoum Assessment Report. Competent Authorities: The Netherlands and Italy, European Union, p. 37.
eCA, 2016b. Coumatetralyl Assessment Report. Competent Authority, Denmark, European Union, p. 40.
eCA, 2016c. Difethialone Assessment Report. Competent Authority, Norway, European Union, p. 39.
eCA, 2016d. Flocoumafen Assessment Report. Competent Authority, The Netherlands, European Union, p. 30.
European Chemicals Agency, 2018. Revised Emission Scenario Document for Product Type 14 (Rodenticides). European Chemicals Agency, Helsinki, Finnland, p. 106.
European Union, 2012. Regulation (EU) No 528/2012 of the European parliament and of the council of 22 May 2012 concerning the making available on the market and use of biocidal products. Off J European Union L 167, 1–128.
Fan, P., Gao, Y., Zheng, M., Xu, T., Schoenhagen, P., Jin, Z., 2018. Recent progress and market analysis of anticoagulant drugs. J. Thorac. Dis. 10 (3), 2011–2025.
Gómez-Canela, C., Barata, C., Lacorte, S., 2014a. Occurrence, elimination, and risk of anticoagulant rodenticides and drugs during wastewater treatment. Environ. Sci. Pollut. Res. 21 (11), 7194–7203.
Gómez-Canela, C., Lacorte, S., 2016. Comprehensive characterization of anticoagulant rodenticides in sludge by liquid chromatography-tandem mass spectrometry. Environ. Sci. Pollut. Res. Int. 23 (15), 15739–15748.
Gómez-Canela, C., Vazquez-Chica, A., Lacorte, S., 2014b. Comprehensive characterization of rodenticides in wastewater by liquid chromatography-tandem mass spectrometry. Anal. Bioanal. Chem. 406 (1), 345–358.
Horak, K.E., Fisher, P.M., Hopkins, B., 2018. In: van den Brink, N.W., Elliott, J.E., Shore, R.F., Rattner, B.A. (Eds.), Pharmacokinetics of Anticoagulant Rodenticides in Target and Non-target Organisms. Springer, Cham, Switzerland, pp. 87–108.
Karakurt, S., Schmid, L., Hübner, U., Drewes, J.E., 2019. Dynamics of wastewater effluent contributions in streams and impacts on drinking water supply via riverbank filtration in Germany - a national reconnaissance. Environ. Sci. Technol. 53 (11), 6154–6161.
Kasprzyk-Hordern, B., 2010. Pharmacologically active compounds in the environment and their chirality. Chem. Soc. Rev. 39 (11), 4466–4503.
Koivisto, E., Koivisto, P., Hanski, I.K., Korkolainen, T., Vuorisalo, T., Karhilahti, A., Välttilä, V., Loivamaa, I., Koivisto, S., 2016. Prevalence of Anticoagulant Rodenticides in Non-target Predators and Scavengers in Finland. Finnish Safety and Chemicals Agency (Tukes), Helsinki, Finnland, p. 41.
Koivisto, E., Santangeli, A., Koivisto, P., Korkolainen, T., Vuorisalo, T., Hanski, I.K., Loivamaa, I., Koivisto, S., 2018. The prevalence and correlates of anticoagulant rodenticide exposure in non-target predators and scavengers in Finland. Sci. Total Environ. 642, 701–707.
Kotthoff, M., Rüdel, H., Jürling, H., Severin, K., Hennecke, S., Friesen, A., Koschorreck, J., 2018. First evidence of anticoagulant rodenticides in fish and suspended particulate matter: spatial and temporal distribution in German freshwater aquatic systems. Environ. Sci. Pollut. Res. Int. 1–11.

Krüger, G., Solas, H., 2010. Neighbours in the sewer network - results of a questionnaire survey on rat control. Korrespondenz Abwasser, Abfall 57 (5), 430–435.
Lin, Y., Shen, X., Yuan, Q., Yan, Y., 2013. Microbial biosynthesis of the anticoagulant precursor 4-hydroxycoumarin. Nat. Commun. 4, 2603–2610.
Masuda, B.M., Fisher, P., Jamieson, I.G., 2014. Anticoagulant rodenticide brodifacoum detected in dead nestlings of an insectivorous passerine. N. Z. J. Ecol. 38 (1), 110–115.
Morrison, S.A., Sieve, K.K., Ratajczak, R.E., Bringolf, R.B., Belden, J.B., 2016. Simultaneous extraction and cleanup of high-lipid organs from white sturgeon (*Acipenser transmontanus*) for multiple legacy and emerging organic contaminants using QuEChERS sample preparation. Talanta 146, 16–22.
Park, B.K., 1988. Warfarin: metabolism and mode of action. Biochem. Pharmacol. 37 (1), 19–27.
Pitt, W.C., Berentsen, A.R., Shiels, A.B., Volker, S.F., Eisemann, J.D., Wegmann, A.S., Howald, G.R., 2015. Non-target species mortality and the measurement of brodifacoum rodenticide residues after a rat (*Rattus rattus*) eradication on Palmyra Atoll, tropical Pacific. Biol. Conserv. 185, 36–46.
Rattner, B.A., Lazarus, R.S., Elliott, J.E., Shore, R.F., van den Brink, N., 2014. Adverse outcome pathway and risks of anticoagulant rodenticides to predatory wildlife. Environ. Sci. Technol. 48 (15), 8433–8445.
Regnery, J., Friesen, A., Geduhn, A., Göckener, B., Kotthoff, M., Parrhysius, P., Petersohn, E., Reifferscheid, G., Schmolz, E., Schulz, R.S., Schwarzbauer, J., Brinke, M., 2019. Rating the risks of anticoagulant rodenticides in the aquatic environment: a review. Environ. Chem. Lett. 17 (1), 215–240.
Ruiz-Suarez, N., Melero, Y., Giela, A., Henriquez-Hernandez, L.A., Sharp, E., Boada, L.D., Taylor, M.J., Camacho, M., Lambin, X., Luzardo, O.P., Hartley, G., 2016. Rate of exposure of a sentinel species, invasive American mink (*Neovison vison*) in Scotland, to anticoagulant rodenticides. Sci. Total Environ. 569–570, 1013–1021.
Santos, L.H., Gros, M., Rodriguez-Mozaz, S., Delerue-Matos, C., Pena, A., Barceló, D., Montenegro, M.C.B., 2013. Contribution of hospital effluents to the load of pharmaceuticals in urban wastewaters: identification of ecologically relevant pharmaceuticals. Sci. Total Environ. 461, 302–316.
Schaar, H., Kreuzinger, N., 2017. 4. Reinigungsstufe auf Kläranlagen zur weitergehenden Behandlung kommunaler Abwässer (in German). Österreichische Wasser- Abfallwirtsch. 69 (7–8), 340–345.
Serieys, L.E.K., Bishop, J., Okes, N., Broadfield, J., Winterton, D.J., Poppenga, R.H., Viljoen, S., Wayne, R.K., O'Riain, M.J., 2019. Widespread anticoagulant poison exposure in predators in a rapidly growing South African city. Sci. Total Environ. 666, 581–590.
Smedes, F., 1999. Determination of total lipid using non-chlorinated solvents. Analyst 124, 1711–1718.
Streit, B., 1998. In: B. E, T., D, H., S, B. (Eds.), Bioaccumulation of Contaminants in Fish. Birkhäuser, Basel, Switzerland.
Teubner, D., Paulus, M., Veith, M., Klein, R., 2015. Biometric parameters of the bream (*Abramis brama*) as indicators for long-term changes in fish health and environmental quality - data from the German ESB. Environ. Sci. Pollut. Res. Int. 22 (3), 1620–1627.
Thomas, K.V., Dye, C., Schlabach, M., Langford, K.H., 2007. Source to sink tracking of selected human pharmaceuticals from two Oslo city hospitals and a wastewater treatment works. J. Environ. Monit. 9 (12), 1410–1418.
Umweltbundesamt, 2019. Authorisation of Anticoagulant Rodenticides in Germany - Risk Mitigation Measures, Best Practice Code and FAQs. German Federal Environment Agency, Dessau-Rosslau, p. 42.
van den Brink, N.W., Elliott, J.E., Shore, R.F., Rattner, B.A. (Eds.), 2018. Anticoagulant Rodenticides and Wildlife. Springer Nature, Cham, Switzerland.
Vudathala, D., Cummings, M., Murphy, L., 2010. Analysis of multiple anticoagulant rodenticides in animal blood and liver tissue using principles of QuEChERS method. J. Anal. Toxicol. 34 (5), 273–279.

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REVIEW

Rating the risks of anticoagulant rodenticides in the aquatic environment: a review

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Abstract

Anticoagulant rodenticides are used worldwide to control commensal rodents for hygienic and public health reasons. As anticoagulants act on all vertebrates, risk is high for unintentional poisoning of terrestrial and aquatic wildlife. Causative associations have been demonstrated for the unintended poisoning of terrestrial nontarget organisms. However, behavior and fate of anticoagulant rodenticides in the aquatic environment have received minimal attention in the past despite considerable acute toxicity of several anticoagulants to aquatic species such as fish. In light of recent regulatory developments in the European Union concerning rodenticides, we critically review available information on the environmental occurrence, fate, and impact of anticoagulant rodenticides in the aquatic environment and identify potential risks and routes of exposure as well as further research needs. Recent findings of anticoagulant rodenticides in raw and treated wastewater, sewage sludge, estuarine sediments, suspended particulate matter, and liver tissue of freshwater fish in the low ng/L and µg/kg range, respectively, demonstrate that the aquatic environment experiences a greater risk of anticoagulant rodenticide exposure than previously thought. While the anticoagulant's mechanism of action from the molecular through cellular levels is well understood, substantial data gaps exist regarding the understanding of exposure pathways and potential adverse effects of chronic exposure with multiple active ingredients. Anticoagulants accumulating in aquatic wildlife are likely to be transferred in the food chain, causing potentially serious consequences for the health of wildlife and humans alike.

Keywords Bioaccumulation · Biocides · Exposure · Second-generation anticoagulant rodenticides · Sewer baiting · Toxicity

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Introduction

In developed countries, rodenticides are primarily used to control commensal rodents such as brown rat (*Rattus norvegicus*), roof rat (*R. rattus*), and house mice (*Mus* spp.) for hygienic and public health reasons, in agricultural animal husbandry, in the food industry, and to a lesser extent for storage and material protection. Rodents pose a hazard to human health because they carry and transmit a vast array of diseases to humans and their domesticated animals (Battersby 2015). A particular problem in industrialized countries is the high number of brown rats in sewer systems of cities, where they find shelter and food. Sewer systems may also serve as hidden pathways for rats to move freely and undiscovered between their nests and potential food sources. Although rats in sewers are not a problem by themselves as they do not damage properly installed and intact pipes, they roam between subsurface and surface, and their population

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must be controlled to prevent health risks or costly damage (Lund 2015).

There are many different biocidal products registered as rodenticides worldwide. They can be grouped together depending on their mode of application, e.g., poisoned bait, poisonous gas, contact foam, as well as speed of action, i.e., acute, subacute, and chronic (Buckle and Eason 2015). Anticoagulant rodenticides are the most effective and commonly used active ingredients of these biocidal products and fall into the category of slow-acting compounds. Anticoagulant rodenticides inhibit the vitamin K epoxide reductase enzyme involved in the blood coagulation process of warm-blooded vertebrates (mammals, birds) and thereby disrupt the recycling of vitamin K_1 (phylloquinone). All anticoagulant rodenticides are either derivatives of 4-hydroxycoumarin or indane-1,3-dione and are structurally similar, but variations exist in their toxicity to target rodents. The exact mechanism of inhibition of clotting caused by hydroxycoumarin-related anticoagulation is described elsewhere (Buckle and Eason 2015; Rattner and Mastrota 2018). An effective dose of anticoagulant rodenticide must be ingested to have a sufficiently prolonged effect in blocking the vitamin K cycle and causing failure of the blood clotting mechanism. Poisoned animals die via internal hemorrhage. Active ingredients such as warfarin, coumatetralyl, and chlorophacinone that were commercialized between 1950 and 1970 are categorized as first-generation anticoagulant rodenticides. The more potent hydroxycoumarin derivatives difenacoum, brodifacoum, bromadiolone, and flocoumafen as well as the thiocoumarin derivative difethialone were developed and marketed in the mid-seventies and mid-eighties, respectively, to overcome warfarin resistance in rodents and are known as second-generation anticoagulant rodenticides. In recent years, ready-to-use loose, paste, and solid bait formulations are predominantly used during chemical rodent control. Bait formulations containing first-generation anticoagulant rodenticides generally require multiple feeding of target organisms until a lethal effect is achieved whereas second-generation anticoagulant rodenticides are more toxic and single feeding is often sufficient for a lethal dose. The delayed action of anticoagulant rodenticides prevents the development of conditioned taste aversion or bait shyness by rodents (Buckle and Eason 2015).

As anticoagulant rodenticides act on all vertebrates, risk is high for unintentional poisoning of wildlife and domesticated animals. Wildlife exposure generally occurs via three pathways: through direct ingestion of rodenticide bait by nontarget species (primary exposure), by take-up of primarily or secondarily exposed individuals through predators or scavengers (secondary and tertiary exposure), or from consumption of terrestrial or aquatic organisms that have been exposed to anticoagulant rodenticides via emissions to the environment (secondary poisoning via environmental emissions). Invertebrates may also be at risk from primary poisoning as a result of bait applications (Liu et al. 2015). Pathways and important aspects of wildlife exposure to anticoagulant rodenticides in the aquatic environment are illustrated in Fig. 1. Second-generation anticoagulant rodenticides were classified as potentially persistent, bioaccumulative, and toxic substances and their release into the environment should be minimized. Despite the consideration of 'candidates for substitution' under European Union legislation, economic relevance of anticoagulant rodenticides in the rodenticide market is still high as no chemical alternatives that are sufficiently effective but less critical are currently approved. However, recent developments gear toward their substitution with less critical active substances. In addition, the implementation of a third generation to minimize ecotoxicological risks associated with the use of second-generation anticoagulant rodenticides without losing their efficacy was suggested (Damin-Pernik et al. 2016, 2017). Currently, alpha-bromadiolone is under evaluation as a new active substance within product type 14 (rodenticides) by the European Chemicals Agency. One important aspect in this development is that the economic viability of anticoagulant rodenticide use for rodent control depends not only on the cost of bait but also on the mode of application and required risk mitigation practices (Jacob and Buckle 2018). In principle, a wide range of risk mitigation measures must be deployed when anticoagulant rodenticides are used.

Environmental exposure to anticoagulant rodenticides may result during manufacture of the active substance, formulation of the biocidal product, application of baits (intended and improper use, respectively), and (inadequate) disposal of baits. Two recently published edited books attempt to gather available information on the environmental risks associated with rodent control using anticoagulant rodenticides and provide comprehensive information on their chemistry and toxicology as well as their environmental impact on terrestrial nontarget wildlife (Buckle and Smith 2015; van den Brink et al. 2018). However, surprisingly little is known about the environmental fate of active ingredients after their release from baits, rodent carcasses and feces during outdoor rodent control in urban and suburban settings, e.g., in and around sewer systems, open space near shorelines, or around buildings and constructions. With the exception of sewers and burrows, deployment of anticoagulant rodenticide containing bait during outdoor rodent control usually happens by using tamper-resistant bait stations to minimize exposure to nontarget organisms and the environment. Nevertheless, a diffuse release of active ingredients and respective transformation and metabolic residues from rodents and other nontarget wildlife via urine and feces may be anticipated around controlled areas. Some second-generation anticoagulant rodenticides are mainly excreted as unchanged compounds, whereas the metabolic

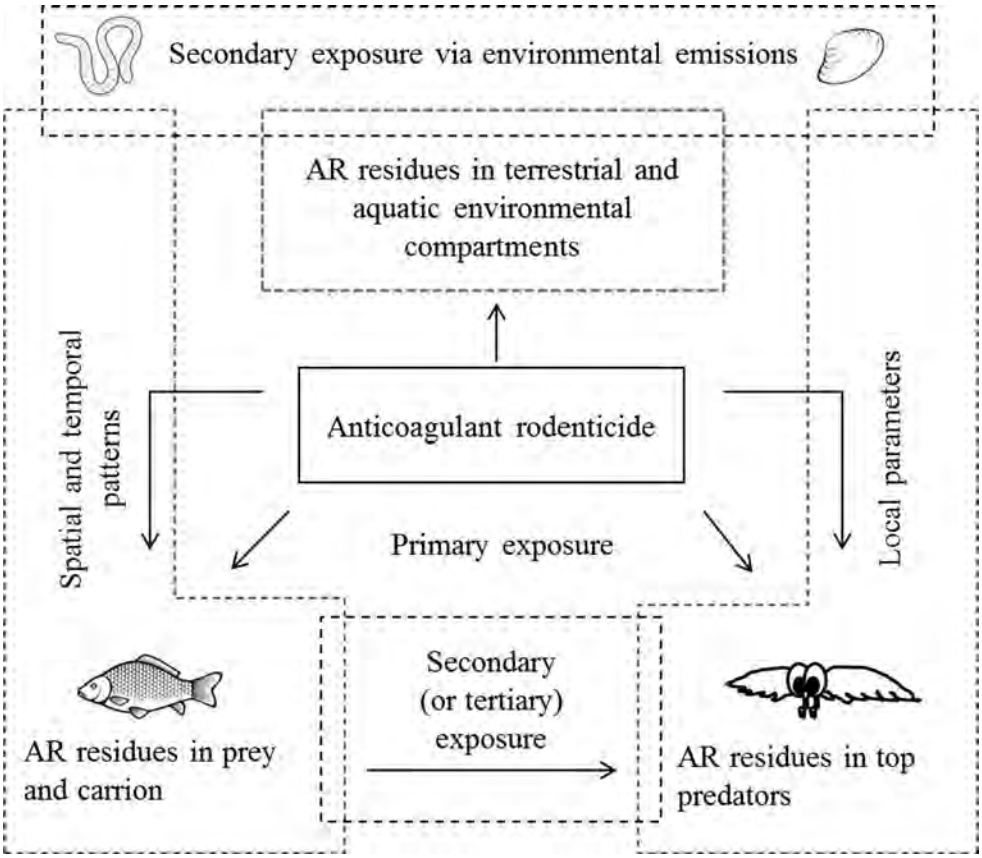

Fig. 1 Pathways and aspects of wildlife exposure to anticoagulant rodenticides (AR) in the aquatic environment adapted from Geduhn (2015). Wildlife exposure generally occurs via three pathways: through direct ingestion of rodenticide bait by nontarget species (primary exposure), by take-up of primarily or secondarily exposed individuals through predators or scavengers (secondary and tertiary exposure), or from consumption of terrestrial or aquatic organisms that have been exposed to anticoagulant rodenticides via emissions to the environment (secondary poisoning via environmental emissions)

transformation of warfarin and chlorophacinone in rats is governed by hydroxylation (Larsen 2003). Baits approved for use in sewers usually consist of wax or fat. As the active ingredients are not chemically bound to the bait material in these product formulations, they will be released upon disintegration of bait blocks during prolonged exposure to moist or wet conditions, e.g., fluctuating water levels in baited manholes, steam. Little information is available about their physical stability and release rates of active ingredient when exposed to moist or wet environments (Nakagawa et al. 2015). Resistance and minimal leaching of weatherproof baits containing brodifacoum even after 500 mm of rainfall was reported by Booth et al. (2010). However, several studies reported the occurrence of anticoagulant rodenticides in sewage sludge (Gómez-Canela and Lacorte 2016), raw and treated wastewater (Gómez-Canela et al. 2014a, b), suspended particulate matter (Kotthoff et al. 2018), estuarine sediments (Cavanagh and Ward 2014), and liver tissue of freshwater fish from impacted streams (Cavanagh and Ward 2014; Kotthoff et al. 2018). These findings suggest that anticoagulant rodenticides might enter the aquatic environment via wastewater treatment plants and direct stormwater discharge into surface water bodies after baiting in and around sewer systems and drainages. Cleaning processes after indoor rodent control operation may also result in (minor) environmental exposure via the sewage system (Larsen 2003). However, in New Zealand there is increasing evidence that anticoagulant rodenticide application for both household rodent control and field pest management contributes to the contamination of aquatic wildlife, presumably through carcasses of poisoned animals entering water bodies, rather than direct contamination by bait (Cavanagh and Ward 2014). Besides biocidal use, pharmaceutical use of vitamin K antagonists should also be taken into account when assessing potential environmental exposure pathways and sources of anticoagulant rodenticides. Oral anticoagulants of the 4-hydroxycoumarin class such as warfarin (trade name Coumadin®), phenprocoumon (Marcumar®, Falithrom®), and acenocoumarol (Sintrom®) are commonly used to treat thromboembolic diseases (Lin et al. 2013).

To overcome the aforementioned knowledge gaps, we critically reviewed available information on the environmental fate and impact of anticoagulant rodenticides in the aquatic environment and direct and indirect routes of exposure. Moreover, we identified potential risks as well as further research needs. Anticoagulants entering the aquatic environment and accumulating in aquatic wildlife are likely to be transferred in the food chain, causing potentially serious consequences for the health of wildlife and humans alike. In light of recent regulatory developments in the

European Union concerning rodenticides, risk mitigation measures and instructions for use of anticoagulant rodenticides are discussed with a focus on Germany. An overview of active substances and products registered worldwide for biocidal use and plant protection is provided elsewhere (Jacob and Buckle 2018).

Regulatory aspects of rodent control in the European Union and Germany

In the European Union, rodenticides need to be authorized prior to being made available on the market. European Union authorization of rodenticides distinguishes between their application as biocides for the protection of human health and manmade materials and plant protection products, respectively. Prior to European Union-wide approval of active substances, they are subject to similar but separate risk assessment processes in either sector within a review procedure involving all European Union Member States. After an active substance is approved, national product authorizations can be granted in compliance with suitable risk mitigation measures. These measures are frequently published in the best practice guidelines at national and international level (UBA 2014; CRRU 2015; EBPF 2015). Because risk mitigation measures are set by each individual member state, a single commercial product may have more than one set of measures attached to its marketing authorizations across Europe (Elliott et al. 2016). Harmonization of anticoagulant rodenticide registration and marketing by combining expertise of registration authorities and streamlining procedures would be worthwhile (Jacob and Buckle 2018). Recently, at least the majority of anticoagulant rodenticide instructions for use and risk mitigation measures were harmonized within the European Union in the context of their re-approval as biocidal active substances in 2016.

The vast majority of rodenticides are applied as biocides. The new European Union Biocidal Products Regulation No. 528/2012 (European Union 2012) regulates the sale, supply, and use of biocidal products throughout the European Union. As of 2018, second-generation anticoagulant rodenticides continue to be authorized under the Biocidal Products Regulation for use as biocides to protect public health due to the lack of safe alternatives (ECHA 2017b). Yet, their re-authorization is subject to a set of strict risk mitigation measures and restrictions regarding their marketing. For example, anticoagulant rodenticide concentrates are solely available to industrial manufacturers, but ready-to-use product formulations can be registered for use by professionals and consumers. In general, anticoagulant rodenticide bait formulations consist of a single active ingredient. Eight active substances belonging to the class of anticoagulants are currently approved in the European Union for biocidal use, thereof three first-generation with maximum permissible concentrations of 0.079% (warfarin), 0.0375% (coumatetralyl), and 0.005% (chlorophacinone), and five second-generation anticoagulant rodenticides with maximum permissible concentrations of 0.0075% (difenacoum), 0.005% (bromadiolone, brodifacoum, flocoumafen), and 0.0025% (difethialone), respectively. The first-generation anticoagulant rodenticide warfarin is concurrently authorized for pharmaceutical use.

In several European Union Member States, bromadiolone (Italy, France, Netherlands, and Romania) and difenacoum (Italy, Portugal) are also approved as active ingredients in plant protection products according to the European Union Pesticides Database (assessed on January 22, 2018). Both compounds are listed as candidates for substitution. Nevertheless, a recent trend across the European Union is to abstain from anticoagulant rodenticides for plant protection and to restrict the use of biocidal second-generation anticoagulant rodenticides to professional users because of human and environmental risks. Hence, companies increasingly tend to register biocidal anticoagulant rodenticide formulations instead of registration in the plant protection sector. In Germany, authorization of plant protection products containing anticoagulants phased out and their domestic sales and exports stopped at the end of 2013 (BVL 2012). During emergency situations in plant protection that cannot be contained by other means, chlorophacinone is still permissible for limited and controlled use, e.g., against local vole outbreaks in 2015 (BVL 2015), with a maximum duration of 120 days according to article 53 of the Plant Protection Products Regulation No. 1107/2009 (European Union 2009). Few anticoagulant rodenticide bait formulations are registered in European Union Member States that contain two active ingredients, e.g., difenacoum and bromadiolone or difenacoum and brodifacoum, to increase potency and circumvent resistance. The majority of biocidal anticoagulant rodenticide products currently authorized in Germany contain difenacoum (51), bromadiolone (41), and brodifacoum (37) followed by warfarin (7), coumatetralyl (5), difethialone (4), chlorophacinone (4), and flocoumafen (3) according to the European Chemicals Agency Biocidal Products Database (assessed on April 11, 2018).

Based on the implementation of national risk mitigation measures, second-generation anticoagulant rodenticides, as of September 2013, may no longer be used in Germany by persons other than trained pest control operators and professional users providing an appropriate proof of qualification in the context of the new European Union Biocidal Products Regulation. Yet, a loophole exists. Despite the restricted use of second-generation anticoagulant rodenticide bait formulations in Germany, consumer sales are still permissible as national legal provisions on the sale of biocides are missing. First-generation anticoagulant rodenticides may still be used by consumers against mice and rats in indoor scenarios and

immediately around buildings. Few solid bait block formulations containing chlorophacinone and warfarin, respectively, are currently authorized for application in sewer systems by professional users. None of the coumatetralyl products is permitted for use in sewer systems. However, with the withdrawal of contact powder formulations from the European market due to safety concerns, an alternative water-based foam formulation containing 0.4% coumatetralyl was authorized for professional users to apply in indoor areas such as access holes, cavity walls, and pipe works.

Due to scientifically proven teratogenic effects of warfarin and an assumed analogy because of similarities in structure and mode of action (Pieper et al. 2014), all anticoagulant rodenticide containing products were recently classified as toxic for reproduction in categories 1A or 1B (European Commission 2016) by the European Chemicals Agency. The classification applies to all products with a concentration of 0.003% (30 ppm) or more of the active substance and will further restrict the range of products authorized for consumer use. Products classified and labeled as toxic for reproduction are only approved for professional users with appropriate certification (European Union 2012). This 9th adaptation of Regulation No. 1272/2008 'Classification, labeling, and packaging of chemical substances' (European Commission 2016) to technical and scientific progress is expected to have consequences for the European rodenticide market. On March 1, 2018, the derogation period ended for the sale of rodenticides for which the labeling does not comply. To circumvent limitations of use in the biocidal sector, a general shift from 0.005% (50 ppm) to less than 0.003% concentration of active ingredient in second-generation anticoagulant rodenticide products is expected as soon as the amendment is taking effect. Besides difethialone, concentrations of brodifacoum and flocoumafen can be reduced to below 0.003% without reducing their effectiveness whereas efficacy of difenacoum, bromadiolone, and first-generation products with less than 0.003% active ingredient is disputed due to observed regional resistance (Buckle and Eason 2015). Along with the active ingredients, anticoagulant rodenticide bait pack sizes are also changing. All baits approved for consumer use in the European Union will have a maximum pack size (European Commission 2017c). With this, a greater distinction between professional and consumer products is intended. It is also intended to prevent consumers from buying and storing large quantities of bait which could cause environmental hazards.

European biocidal anticoagulant rodenticide market

Due to the European Chemicals Agency implemented policies restricting rodent pest management by chemical rodenticides almost entirely to anticoagulants, they account for the largest market share on the European biocidal rodenticide market in recent years. On the contrary, a wider range of non-anticoagulants is available under the United States Environmental Protection Agency on the US rodenticide market (Jacob and Buckle 2018). Nevertheless, about 95% of the chemical control of rodents in the USA is carried out using anticoagulants (Liphatech 2013). Estimates on anticoagulant rodenticide sales are in the hundreds of millions of dollars annually in the USA and European countries (Rattner et al. 2014). Market research data valued the European rodenticide market at 226 million euros in 2016 and insinuated that the strict regulation on the use of rodenticides within the European Union led to stationary market growth in the past few years. As of late 2017, market analysts projected a compound annual growth rate of 5.77% over the next 5 years, which will likely be driven by the non-anticoagulant rodenticides segment (Market Data Forecast 2017).

In contrast to active ingredients used in plant protection products within the European Union, disclosure of biocide sales and use data is not required by European law. Unfortunately, national and global rodenticide market data are mostly considered confidential business information and up-to-date, open access national or European Union-wide biocidal anticoagulant rodenticide sales data under the new Biocidal Products Regulation are scarce (Elliott et al. 2016; Jacob and Buckle 2018). Compared with other pest control and plant protection products, the market for anticoagulant rodenticides is comparatively small and actual quantities of active ingredients applied as biocides appear minor compared to major pesticides and pharmaceuticals (Endepols 2002). Anticoagulant rodenticides accounted for approximately 3% of registered biocidal products in Germany in 2014 (Schmolz et al. 2014). Based on consumer research market data from 2012 (Parker 2013), the annual national use of anticoagulant rodenticides by pest control professionals in Germany was estimated to exceed 1000 metric tons of bait material, i.e., expenses of 10 million euros on anticoagulant rodenticide containing products by professional users. This represented roughly 50 kg of active ingredients (Schmolz et al. 2014). While existing data suggest that pest control professionals are among the main users of biocidal anticoagulant rodenticides in Germany, other important user groups are agribusinesses, local authorities, and household consumers (Barten 2014). In comparison, the total amount of anticoagulant rodenticides sold in Finland in 2014 was in the range of 250 metric tons based on annual sales volumes collected by the Finnish Safety and Chemicals Agency. Notably, only 5% thereof were supposedly used by pest control professionals in 2014 according to a survey that covered approximately 75% of pest control technicians operating in Finland (Koivisto et al. 2016).

Given the non-disclosure of detailed market sales data, extensive sectoral surveys shed further light on rodenticide usage patterns within the European Union (Murphy

and Oldbury 2002; Dawson and Garthwaite 2004; Krüger and Solas 2010; Hughes et al. 2013; Wardlaw et al. 2016, 2017). Krüger and Solas (2010) conducted a survey among 508 municipalities in Germany in 2010 to gain insight into rat control in and around municipal sewer systems. The participating municipalities represented a population of approximately 15.3 million residents. Person equivalents of the surveyed municipalities ranged between less than 5000 and more than 100,000. Of the municipalities surveyed, 309 provided utilizable information regarding the use of anticoagulant rodenticide containing baits in their sewer systems. The annual domestic use of anticoagulant rodenticides in sewer baiting scenarios was projected as 870.5 metric tons of bait material and 50.3 kg of active ingredients, respectively. About 88% of surveyed municipalities employed pest control in and around their sewer systems, either through contracted pest control professionals or qualified staff. If prorated irrespective of person equivalents and sewage load, each of the approximately 300 municipalities surveyed applied on average 18.4 and 8.4 g/year active ingredient of second-generation and first-generation anticoagulant rodenticides, respectively. Bromadiolone had the highest proportion of 50%, followed by 30% difenacoum and 18% brodifacoum (Krüger and Solas 2010). On the contrary, very little use of anticoagulant rodenticides in sewer baiting scenarios was encountered in a recent Scottish survey representing 81% (4.37 million) of the Scottish population. Only 20% of the respondent local authorities reported sewer baiting activities with a total combined use of 34 kg bait material, i.e., less than 0.2 g active ingredient. Bromadiolone, difenacoum, and brodifacoum were the three most commonly used anticoagulants that were reported in sectoral surveys from the UK and Finland (Dawson and Garthwaite 2004; Koivisto et al. 2016; Wardlaw et al. 2016, 2017). Among the second-generation anticoagulant rodenticides, difenacoum, bromadiolone, and brodifacoum are estimated to have the highest market shares in Germany and France (Fig. 2). Yet, establishing a relationship between anticoagulant rodenticide market shares and their environmental occurrence is not straight forward given the lack of comprehensive data. For instance, the proportion of individuals burdened with different active substances is not expected to mirror national usage patterns exactly due to differences in persistence, bioaccumulation, and elimination profiles (Hughes et al. 2013). In addition, carryover of active ingredient in the manufacture line was observed when bait formulations with different active ingredients were processed in the same facility. Tosh et al. (2012) detected brodifacoum as a contaminant in four different ready-to-use loose bait formulations of the same brand that were not supposed to contain brodifacoum as active ingredient, constituting on average 9.8% (7.7–13.2%) of the total active ingredient detected in the bait. Levels of brodifacoum contamination ranged from 63 to 197 mg/g bait. Thus, brodifacoum residues were also detected in target organisms that consumed the contaminated baits (Tosh et al. 2012).

As mentioned before, pharmaceutical use of vitamin K antagonists should also be taken into account. The global warfarin market was valued at 300 million dollars in 2008 (Lin et al. 2013). Commissioned market research data by Oktay (2015) suggest that warfarin prescriptions declined from 87.5 to 72% through 2008–2014. Pharmaceutical use of warfarin as a blood-thinning agent is still widespread in the USA and the UK, whereas phenprocoumon (Germany, Austria, Belgium, Denmark, The Netherlands, and Switzerland) and acenocoumarol (Italy and Spain) are mainly used across continental Europe. For example, warfarin prescriptions in the UK averaged 800 kg annually between 2004 and 2008 (Kasprzyk-Hordern 2010). Pharmaceutical use of phenprocoumon and warfarin in Germany in 2016 can be roughly extrapolated to a total of 1226 kg and 31 kg of active

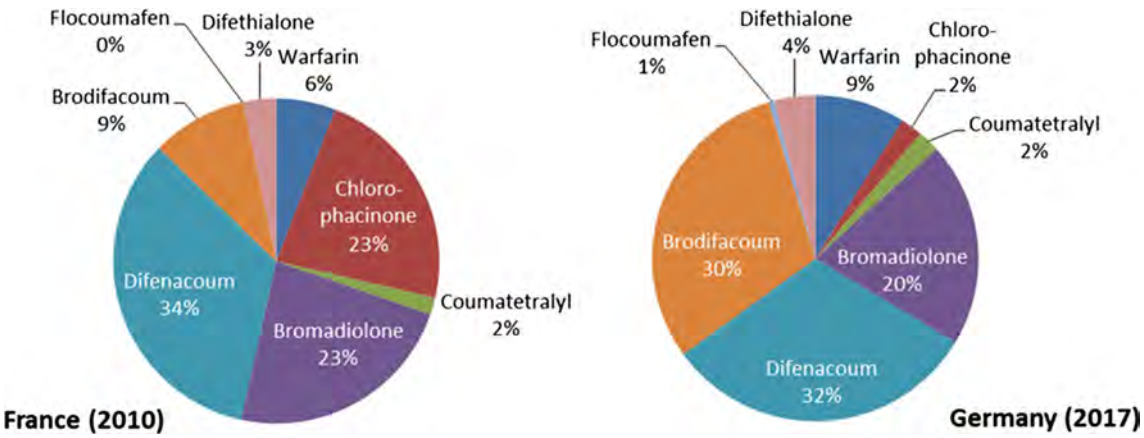

Fig. 2 Estimated market shares of anticoagulant rodenticide active ingredients in France and Germany based on registered commercial biocidal products in France and Germany in 2010 and 2017 adapted from Berny et al. (2010) and Kotthoff et al. (2018), respectively

ingredient, respectively, based on healthcare membership numbers and prescription statistics (UBA 2011; Schwabe et al. 2017).

Predicted environmental emissions

Aside from primary and secondary poisoning of terrestrial nontarget organisms after bait application (Liu et al. 2015; Alomar et al. 2018), very little is known about direct and indirect routes of exposure as well as anticoagulant's distribution and fate in the aquatic environment (Fisher et al. 2012; Masuda et al. 2015). Professional pest control companies, which are among the main users of second-generation anticoagulant rodenticides in urban settings, apply rodenticides commonly 'in and around buildings' (warehouses, agribusinesses), municipal sewer systems, and public open space (Schmolz et al. 2014). Several studies hypothesized that the application of anticoagulant rodenticide containing baits in municipal sewer systems is a major emission source of anticoagulants in urban areas (Gómez-Canela et al. 2014a; Kotthoff et al. 2018). From the sewers, exposure of the aquatic environment most likely occurs via wastewater treatment plant effluents if anticoagulants are not efficiently removed during conventional wastewater treatment. Moreover, stormwater overflow structures in combined sewer systems that discharge highly diluted but untreated sewage directly into receiving surface waters when precipitation causes a surcharge within the system might pose another route. As a result, poisoned rodent carcasses might be flushed from their hiding places in the sewers directly into receiving streams, bypassing mechanical removal at the wastewater treatment plant.

In Germany, all professional users (as well as consumers) are obligated to follow national best practice guidelines for the application of rodenticides which have been implemented within the national biocidal product authorization. Ideally, non-chemical methods and products containing the least potent active ingredient should be used first to control pests. Apart from exceptional cases where difenacoum or bromadiolone containing bait may be constantly applied, permanent deployment of anticoagulant rodenticide containing baits to prevent rodent infestation or to monitor rodent activities is usually not permitted (European Commission 2017a, b). This and the considerable costs associated with rodent control motivated sewer baiting regimes to switch to pulsed baiting instead of surplus baiting. Colvin et al. (1998) demonstrated that sewer baiting requires a systematic approach with close review and adjustments of the baiting strategy based on the quantities and geographic patterns of bait consumption to successfully manage a rat population. Moreover, ineffective use of rodenticides can be misdiagnosed as resistance. According to Gras et al. (2012), surface infestation is not necessarily a reliable indicator of sewer infestation. To comply with national best practice guidelines, inspection of deployed baits after 2 weeks is mandatory during sewer baiting campaigns. Likewise, the collection and appropriate disposal of remaining bait and rodent carcasses is mandated to minimize the risks of environmental exposure (UBA 2014). Yet, nationwide compliance with these guidelines is difficult to assess and control. It has been assumed that the typical use of anticoagulants commonly violates the use instructions for rodenticides (Koivisto et al. 2016). Thus, the exact whereabouts of marketed quantities of active ingredients remain unclear.

In the context of the European Union project EUBEES 2 titled 'Gathering, review and development of environmental emission scenarios for biocides' (Larsen 2003), a method was established to estimate the initial release of anticoagulants from biocidal products to the primary receiving environmental compartments air, soil, and water, including separate calculations for emissions under normal and realistic worstcase conditions (available at http://echa.europa.eu/en/guidance-documents/guidance-on-biocides-legislation/emission-scenario-documents). This guideline is currently under revision. Further guidance on rodenticide emission pathways and the estimation of predicted environmental concentrations in receiving environmental compartments is provided by the European Chemicals Agency (ECHA 2017a). In general, degradation and distribution processes are taken into consideration for the calculation of predicted environmental concentrations for the aquatic compartment.

Worstcase aquatic and terrestrial predicted environmental concentrations of anticoagulant rodenticides based on default values in the emission-scenario document are summarized in Table 1. Very limited information is available regarding predicted environmental concentrations in fish (oral, predator). The suggested predicted environmental concentration of difethialone in whole fish based on wet weight is 6 µg/kg (eCA2016h) and 0.245 µg/kg for difenacoum (eCA 2016g). For difenacoum, it was assumed that secondary poisoning via the aquatic food chain would not be significant due to low water solubility and high adsorption tendency (eCA 2016g).

Due to stricter regulations within the European Union, the use of sewage sludge as fertilizer in agriculture has declined over the past decade. Sewage sludge is increasingly subject to energy recovery, e.g., anaerobic digestion followed by incineration, or thermal waste treatment. Organic compounds adsorbed to the sludge will decompose during incineration, representing a possible sink. This will likely affect the potential exposure of agricultural soils with anticoagulant rodenticides via this route (Table 1). Over the last couple of years, incineration of sludge substantially increased in Germany and a ban on using sewage sludge as fertilizers in agriculture beyond January 1, 2025 (at least for municipal

Table 1 Worstcase predicted environmental concentrations of selected rodenticides after exposure of environmental compartments via wastewater treatment plant (WWTP) discharge and sludge application, respectively, based on default values in the sewer emission scenario according to European Union Competent Authority Assessment Reports

	WWTP influent (ng/L)	Surface water (ng/L)	Groundwater (pore water) (ng/L)	Sediment (µg/kg)	Agricultural soil (µg/kg)	References
Warfarin	63.9	6.39	–	0.0225	0.0159	eCA (2016f)
Chlorophacinone	96	9.6	0.6	–	–	eCA (2016d)
Bromadiolone	62	6.2	–	–	0.72	eCA (2016e)
Brodifacoum	64	1.4	0.9	1.5	1.9	eCA (2016c)
Difethialone	7.2	0.72	–	–	0.06	eCA (2016h)

wastewater treatment plants with more than 50,000 person equivalents) is planned.

Physicochemical properties and environmental fate and impact of anticoagulant rodenticides

Chemical structures and selected physicochemical properties of first- and second-generation anticoagulant rodenticides discussed in this review are summarized in Fig. 3 and Table 2. All of these compounds are either derivatives of indane-1,3-dione or 4-hydroxycoumarin. Despite the similarity of their structures, differences in the physicochemical properties of these compounds exist (Table 2).

Stereochemistry

Chlorophacinone, like coumatetralyl and warfarin, contains one optically active carbon and therefore exists as two enantiomers. Furthermore, chlorophacinone has a *β*-tricarbonyl system resulting in keto-enol tautomerism (Medvedovici et al. 1997). While the ratio of the enantiomers in chlorophacinone formulations is classified as proprietary information (eCA 2016d), commercially available coumatetralyl and warfarin are generally a racemic mixture of R and S enantiomers containing equal parts of each isomer (eCA 2016b, f). Studies of the metabolic fate of the R and the S isomers of warfarin revealed that the two isomers were metabolized by different routes. Furthermore, S warfarin was shown to be five times more potent than R warfarin (Lewis et al. 1974).

Second-generation anticoagulant rodenticides such as bromadiolone, difenacoum, brodifacoum, difethialone, and flocoumafen have two asymmetric carbons in their chemical structure allowing them to exist in two diastereomeric forms (*cis*- and *trans*-isomers) and thus four enantiomeric species. Commercially available second-generation anticoagulant rodenticides are generally a mixture of their *cis*- and *trans*-isomers. *Trans*-isomers are the major diastereomeric form (70–90%) in commercialized bromadiolone (eCA 2016e), whereas flocoumafen, difenacoum, and brodifacoum are a mixture of approximately 50–80% *cis*-isomers and 20–50% *trans*-isomers (eCA 2016a, c, g). Commercial difethialone consists of more than 70% *cis*-isomers (eCA 2016h). Specifics regarding diastereomer ratios in commercial products as well as reasons thereof are mostly treated as proprietary information by manufacturers. As observed for the R and S isomers of warfarin, diastereomers of second-generation anticoagulant rodenticides have slightly different chemical and physical properties and likely have different biological activities (Hauck et al. 2016; Fourel et al. 2017a, b).

Fate and behavior in the environment

Water solubility of anticoagulant rodenticides at 20 °C and neutral pH is generally low, ranging between 267 and 460 mg/L for first-generation and 0.1–18.4 mg/L for second-generation anticoagulant rodenticides, respectively. Most anticoagulants were shown to be hydrolytically stable in water under environmentally relevant conditions, i.e., half-lives exceeding 1 year, and were not expected to partition to the atmosphere due to their low vapor pressure. However, very short photolytic half-lives, i.e., less than 1 day, of most second-generation anticoagulant rodenticides in water under sunlight exposure had been predicted or observed in previous assessments (Table 2). Estimated partition coefficients indicate substantial lipophilicity and bioaccumulation potential of second-generation anticoagulant rodenticides at neutral pH (Table 2). Of the targeted active ingredients, difenacoum, chlorophacinone, difethialone, and flocoumafen exhibit the highest organic carbon adsorption coefficients, warfarin the lowest (Table 2). Notably, second-generation anticoagulant rodenticides possess at least one polar group that can potentially ionize at neutral pH. However, the lipophilic character of brodifacoum, difethialone, and flocoumafen might prevent their ionization in natural aqueous environments. Previous studies demonstrated the effect of both pH and ionic strength on the mechanism of association of anticoagulant rodenticides with humic acid, a natural organic component of soils and sediments, by use of a C_{18} stationary phase (Andre et al. 2004, 2005). A strong tendency of the undissociated portion of the molecule to adsorb to organic matter combined with

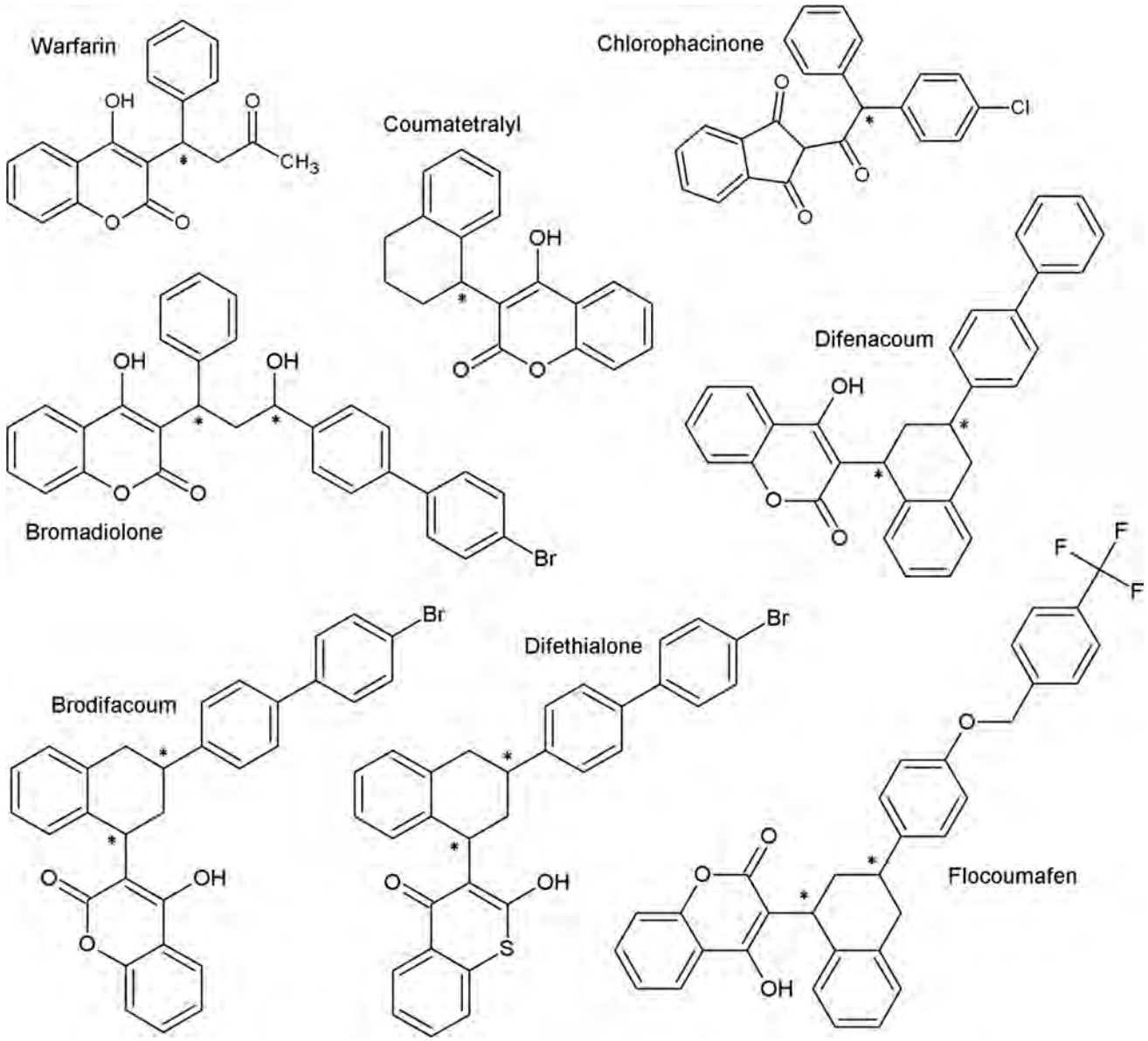

Fig. 3 Chemical structures of first- and second-generation anticoagulant rodenticides authorized in the European Union. The chiral centers of each compound are marked with an asterisk (*)

low water solubility and a high degree of photo-instability means that second-generation anticoagulant rodenticides are unlikely to remain in the water column of surface waters. Thus, their residues are more likely to persist and accumulate in aquatic compartments such as suspended particulate matter, (organic-rich) sediments, and biological tissue of aquatic organisms.

Available information on the route and rate of degradation in aerobic natural sediment water systems is summarized in European Union Competent Authority Assessment Reports (eCA 2016a, b, c, d, e, f, g, h). For brodifacoum, immediate adsorption to the sediment was noted followed by slow transformation with low levels of degradation products, i.e., less than 10% of the applied active substance. Brodifacoum was not expected to accumulate in sediments (eCA 2016c). Bromadiolone was shown to be fairly quickly degraded in soil under aerobic conditions with an estimated dissipation half-time of several days. However, its main metabolite bromadiolone ketone, which likely has a similar level of toxicity as bromadiolone, persisted in the soil in substantial quantities (eCA 2016e). Warfarin degraded fairly quickly in soils under aerobic and ambient temperature conditions after a short lag period (Lao and Gan 2012). Information on flocoumafen degradation rates in sediment water systems is lacking. Based on its low biodegradation potential in soil, i.e., half-life of 213 days at 20 °C, and high hydrolytical

Table 2 Selected physicochemical properties such as molecular weight (MW), water solubility, *n*-octanol—water partition coefficient (Log P_{OW}), acid dissociation constant (pK_a), soil organic carbon adsorption coefficient (Log K_{OC}), and photolytic half-life in water of first- and second-generation anticoagulant rodenticides adapted from European Union Competent Authority Assessment Reports (eCA 2016a, b, c, d, e, f, g, h)

Compound	Molecular formula	MW (Da)	Water solubility* (mg/L)	Log P_{OW} (pH 7)	pK_a	Log K_{OC}	Photolytic half-life in water (h)
First generation							
Coumatetralyl	$C_{19}H_{16}O_3$	292.3	460	1.5	3.9	2.2–2.4	8
Warfarin	$C_{19}H_{16}O_4$	308.3	267	0.7	5.19	2.42	≥ 54 days
Chlorophacinone	$C_{13}H_{15}ClO_3$	374.8	344	2.42	3.4	5.0	24–48
Second generation							
Difenacoum	$C_{31}H_{24}O_3$	444.5	1.7	4.78	4.84	5.23	< 8
Brodifacoum	$C_{31}H_{23}BrO_3$	523.4	0.06–0.2	4.9–8.5	4.5[a]	4.0–4.7	< 24
Bromadiolone	$C_{30}H_{23}BrO_4$	527.4	18.4	3.8–4.1	4.5[a]	3.2–4.2	0.2
Difethialone	$C_{31}H_{23}BrO_2S$	539.5	0.4	6.29	[b]	3.2–8.0	0.4–1
Flocoumafen	$C_{33}H_{25}F_3O_4$	542.5	0.1	6.12	4.5[a]	5.0	38

*At 20 °C and pH 7

[a]Predicted. Not feasible to experimentally determine the dissociation constant due to low water solubility

[b]Not considered ionizable due to low water solubility

stability, flocoumafen is considered to be very persistent in water and sediment (eCA 2016a).

Toxicity and bioaccumulation in aquatic organisms

Recent reviews provide a comprehensive overview on toxicity and pharmacokinetics such as absorption, distribution, metabolism/biotransformation, and excretion of anticoagulant rodenticides in target and terrestrial nontarget organisms (McLeod and Saunders 2013; Horak et al. 2018; Rattner and Mastrota 2018). Anticoagulants bind strongly to vitamin K epoxide reductase. As the liver contains high levels of this protein, it is the main organ of accumulation and storage of anticoagulants. In general, they are eliminated in a biphasic process, with the rapid initial elimination of circulating compounds, followed by slower elimination from binding sites (Huckle et al. 1988). Although anticoagulants have been in use for decades, relatively little is known about their pharmaco- and toxicokinetics in aquatic organisms as well as effects of chronic exposure with multiple active ingredients. Studies about anticoagulant rodenticide exposure in terrestrial nontarget wildlife frequently report the presence of multiple second-generation anticoagulant rodenticides in a single individual, and occasionally a combination of first and second generation. The toxicity of multiple anticoagulant rodenticides in a single organism is expected to be on principal additive. Studies showed that the efficacy to inhibit the vitamin K epoxide reductase activity was similar between most second-generation anticoagulant rodenticide diastereomers in rodents, but different half-lives and persistence behaviors in biological tissues were observed between *cis*- and *trans*-isomers (Damin-Pernik et al. 2016, 2017; Fourel et al. 2017a). According to Fourel et al. (2017b), bromadiolone *cis*-stereoisomer, the minor component in commercial bromadiolone, did not contribute to the toxicity of the active ingredient in red kite due to metabolic differences in rodents and raptors. Lately, hepatic anticoagulant rodenticide residues above 100–200 µg/kg wet weight have been associated with mortalities in terrestrial nontarget organisms (Fourel et al. 2017b). A study about effects of chronic low-level brodifacoum exposure on the feline immune response, however, indicated species-specific anticoagulant insensitivity. Specific pathogen-free domestic cats did not exhibit any clinical signs of brodifacoum intoxication despite elevated hepatic levels of brodifacoum in the range of 1.67–1.94 mg/kg wet weight (Kopanke et al. 2018). In toxicokinetic studies with rats, brodifacoum showed a high potential for bioaccumulation. In all studies undertaken and at all dose levels tested, the liver retained the largest percentage of the dose, even very long time after dosing. Fisher et al. (2003) showed biphasic elimination of brodifacoum from rat liver, consisting of a more rapid initial phase up to 8 days after dosing, and a slower terminal phase. The liver-elimination half-life in rat was 113.5 days for brodifacoum and 26.2 days for warfarin. Moreover, toxicokinetic data suggest that brodifacoum may be more persistent, with a longer liver retention phase than bromadiolone and difenacoum (Hughes et al. 2013). Presumably, high-single-dose-potency second-generation anticoagulant rodenticides persist in the liver for more than 1 year (Fisher et al. 2003).

Today, the embryotoxic potential of warfarin is well accepted (Weigt et al. 2012; Buckle and Eason 2015). On

the contrary, other anticoagulants with similar structures and mode of action have disputed embryotoxic potential (Buckle and Eason 2015). Nevertheless, embryotoxicity induced by bromadiolone exposure at a dose of 350 µg/L was demonstrated in the amphibian model organism African clawed frog (*Xenopus laevis*) adhering frog embryo teratogenesis assay—Xenopus standards (Ondracek et al. 2015). Teratogenicity and embryonic lethality in zebrafish (*Danio rerio*) under acute warfarin exposure at elevated concentrations of greater than or equal to 400 µM (123 mg/L) were reported by Weigt et al. (2012). Fernandez et al. (2014) showed that zebrafish larvae with chronic exposure to a 25-fold lower warfarin concentration experienced significant lethal and sublethal effects, such as hemorrhages, vascular calcification, and skeletal deformities. Interestingly, warfarin demonstrated no significant, measurable metabolism in native rainbow trout liver S9 fractions at a substrate concentration of 1 µM (308 µg/L) (Connors et al. 2013). Yet, a rapid decrease in warfarin levels to below the detection limit was observed in rainbow trout (*Oncorhynchus mykiss*) in less than 11 days after termination of warfarin exposure in a bioconcentration test (eCA 2016f). Connors et al. (2013) pointed to the possibility for tissue-specific expression of cytochrome isozymes involved in warfarin metabolism in fish, e.g., in the gills. No effect on the tested endpoint lethality was observed for rainbow trout when exposed to coumatetralyl at the 5 µg/L level over the duration of 21 days. Furthermore, quick depuration in fish with a dissipation half-live of approximately 14.5 h and low bioaccumulation potential was reported (eCA 2016b). It is presumed that the low-single-dose-potency anticoagulant warfarin persists in the liver for up to 1 month, whereas the moderate-single-dose-potency anticoagulant rodenticide coumatetralyl persists in liver for approximately 6 months (Fisher et al. 2003).

Due to considerable acute toxicity to aquatic species (Table 3) and high mortalities during bioconcentration tests, experimentally derived bioconcentration factors in fish are not available for all anticoagulants. Flocoumafen is considered very bioaccumulative because of its high bioconcentration factor of 24,300 (Table 4). The calculated brodifacoum bioconcentration factor of 35,648 in fish is also very high. The estimated depuration time of brodifacoum in whole fish according to the Organization for Economic Co-operation and Development guideline 305 using a Log P_{OW} of 6.12 is approximately 8 days (50% dissipation) and 34 days (95% dissipation), respectively (eCA 2016c). For bromadiolone and difenacoum, experimentally derived bioconcentration factors in fish were below the threshold of 2000 which defines bioaccumulative and very bioaccumulative (greater than 5000) substances according to European Union regulation No. 253/2011 (European Commission 2011). Bromadiolone exhibited a depuration time of more than 14 days to achieve 50% dissipation. Notably, the experimental bioconcentration factor of difenacoum in fish is lower than estimations based on the *n*-octanol—water partition coefficient (Table 4).

Unfortunately, no detailed information is available regarding second-generation anticoagulant rodenticide uptake and metabolism in fish. In an aquarium feeding trial by Empson and Miskelly (1999), 60 individuals of the marine fish species blue cod (*Parapercis colias*), spotty (*Notolabrus celidotus*), and variable triplefin (*Forsterygion varium*) were exposed to brodifacoum containing bait pellets for 1 h before being transferred to clean holding tanks for 3–4 weeks. After the experiment was terminated, 5% of fish showed hepatic brodifacoum residues according to the authors but no concentrations or reporting limits were provided (Empson and Miskelly 1999). Whole-body brodifacoum residues above 200–300 µg/kg wet weight were associated with mortalities in nontarget coastal marine fish (Pitt et al. 2015).

Analytical methods for anticoagulant rodenticides in environmental samples

Extraction and cleanup

Suitable extraction methods for individual anticoagulant rodenticide residues or mixtures thereof from environmental samples include a wide range of techniques, e.g., liquid–liquid extraction, solid–liquid extraction, and solid-phase extraction, depending on analyte-specific properties (Table 2) and sample type, e.g., biological tissue, sewage, soil/sediment, and water. Optimization of important parameters like composition, type, and pH of extraction solvents, solid/liquid rate volume of extraction solvents, and number of extraction cycles is crucial for each anticoagulant rodenticide residue to facilitate efficient and exhaustive extraction, especially when covering a wide range of different compounds. Traditional high-volume solvent extraction methods, e.g., pressurized liquid extraction, microwave-assisted extraction, and Soxhlet extraction, are frequently substituted by miniaturized extraction methods aiming at minimizing costs of sample preparation while reducing consumables and waste. In particular, the emergence of rapid multi-class, multi-residue analysis methods propelled the development of efficient, rapid, and simple sample preparation techniques. However, regardless of extraction technique, environmental samples (especially biological tissues and sewage) often yield complex extract matrices requiring extensive cleanup to remove co-extracted residues, e.g., lipids and proteins that interfere with quantitative analysis (Goldade et al. 1998; Huerta et al. 2012; Morrison et al. 2016).

Imran et al. (2015) reviewed published extraction and cleanup methods for anticoagulant rodenticides from

Table 3 Toxicity data for most sensitive aquatic species of the groups fish, invertebrates, algae, and microorganisms, respectively. Toxicity endpoints within a defined period of exposure include lethality (L), immobilization (I), growth inhibition (Gi), and respiration inhibition (Ri), respectively

Compound	Aquatic species	Time-scale (h)	End point	Toxicity	Refs.
Brodifacoum	*Oncorhynchus mykiss*	96	L	LC_{50}: 0.04 mg/L; 0.042 mg/L	eCA (2016c)
	Daphnia magna	48	I	EC_{50}: 0.25 mg/L	
	Selenastrum capricornutum	72	Gi	E_rC_{50}: 0.04 mg/L	
	Activated sludge	3	Ri	EC_{10}: > 0.058 mg/L	
Bromadiolone	*Oncorhynchus mykiss*	96	L	LC_{50}: > 8.0 mg/L; 2.86 mg/L	eCA (2016e)
	Daphnia magna	48	I; L	EC_{50}: 5.79 mg/L; LC_{50}: 2.0 mg/L	
	Pseudokirchneriella subcapitata	72	Gi	E_rC_{50}: 1.14 mg/L	
	Activated sludge	3	Ri	EC_{50}: 31.6 mg/L; 132.8 mg/L	
Difenacoum	*Oncorhynchus mykiss*	96	L	LC_{50}: 0.065 mg/L; 0.33 mg/L	eCA (2016g)
	Daphnia magna	48	L	LC_{50}: 0.52 mg/L; 0.91 mg/L	
	Selenastrum capricornutum	72	Gi	E_rC_{50}: 0.8 mg/L; 0.51 mg/L	
	Pseudomonas putida	6	Ri	EC_{50}: > 2.3 mg/L; > 999.7 mg/L	
Flocoumafen	*Oncorhynchus mykiss*	96	L	LC_{50}: 0.07 mg/L	eCA (2016a)
	Daphnia magna	48	I	EC_{50}: 0.18 mg/L	
	Pseudokirchneriella subcapitata	72	Gi	E_rC_{50}: > 18.2 mg/L	
	Activated sludge	3	Ri	EC_{50}: > 4.0 mg/L	
Difethialone	*Oncorhynchus mykiss*	96	L	LC_{50}: 0.051 mg/L	eCA (2016h)
	Daphnia magna	48	I	EC_{50}: 0.0044 mg/L	
	Selenastrum capricornutum	72	Gi	E_rC_{50}: > 0.18 mg/L	
	Activated sludge	3	Ri	EC_{50}: > 100 mg/L	
Warfarin	*Salmo gairdniri*	96	L	LC_{50}: 65 mg/L	eCA (2016f)
	Daphnia magna	48	I	EC_{50}: > 105 mg/L	
	Scenedesmus subspicatus	72	Gi	E_rC_{50}: > 83.2 mg/L	
	Activated sludge	2.9	Ri	EC_{20}: > 400 mg/L	
Coumatetralyl	*Salmo gairdniri*	96	L	LC_{50}: 53 mg/L	eCA (2016b)
	Daphnia magna	48	I	EC_{50}: > 14 mg/L	
	Scenedesmus subspicatus	72	Gi	E_rC_{50}: > 18 mg/L	
	Activated sludge	24	Ri	EC_{50}: 4210 mg/L	
Chloro-phacinone	*Oncorhynchus mykiss*	96	L	LC_{50}: 0.45 mg/L	eCA (2016d)
	Daphnia magna	48	I	EC_{50}: 0.64 mg/L	
	Desmodesmus subspicatus	72	Gi	E_rC_{50}: 2.2 mg/L	
	Activated sludge	3	Ri	EC_{50}: > 1000 mg/L	

L lethality, *I* immobilization, *Gi* growth inhibition, *Ri* respiration inhibition, LC_{50} lethal concentration for 50% of test subjects, EC_{50} effective concentration for 50% of test subjects, E_rC_{50} concentration resulting in 50% growth rate reduction, EC_{20} effective concentration for 20% of test subjects, EC_{10} effective concentration for 10% of test subjects

biological tissues and discussed extraction performances as well as limitations. Several recent studies utilized ultrasound-assisted extraction to extract various pharmaceutical and/or biocidal anticoagulants from aquatic organisms (Magiera et al. 2015; de Solla et al. 2016; Kotthoff et al. 2018), sludge (Gómez-Canela and Lacorte 2016), suspended particulate matter (Kotthoff et al. 2018), and soil (Hernández et al. 2013). Reversed phase solid-phase extraction on various stationary phases was carried out for enrichment and cleanup of anticoagulants in aqueous samples such as raw wastewater, treated wastewater, surface water, and groundwater (Fisher et al. 2012; Gómez-Canela et al. 2014b; Watkins et al. 2014; Wode et al. 2015). Several anticoagulants were also sufficiently extracted from spiked water samples employing liquid–liquid extraction with ethyl acetate (Hernández et al. 2013; Gómez-Canela et al. 2014b). When Gómez-Canela et al. (2014b) investigated anticoagulant rodenticides in wastewater, better performance regarding the number of detected residues, recoveries, and reproducibility was achieved using solid-phase extraction on hydrophilic–lipophilic balanced or weak anion polymeric sorbent, respectively, compared to miniaturized liquid–liquid

Table 4 Estimated and measured bioconcentration factors (BCF) of first- and second-generation anticoagulant rodenticides in fish

Compound	Estimated BCF^{*}_{fish} (L/kg)	Estimated BCF^{a}_{fish} (L/kg)	Estimated BCF^{b}_{fish} (L/kg)	Measured BCF^{c}_{fish} (L/kg)
First generation				
Warfarin	1.0	23.9	–	≤21.6
Chlorophacinone	19.8	492	22.75	–
Coumatetralyl	2.0	358	–	11.4
Second generation				
Bromadiolone	108	–	339; 575	460
Brodifacoum	1296	–	35,648	–
Difenacoum	451	9010	35,645	1100
Difethialone	2949	14,000	39,974	–
Flocoumafen	1003	–	36,134	24,300

*Estimated at pH 7.4 using ACD/Labs software v8.14

[a]Estimated using BCFWIN v2.17 US Environmental Protection Agency

[b]Adapted from EU Competent Authority Assessment Reports (eCA 2016a, c, d, e, g, h)

[c]Adapted from EU Competent Authority Assessment Reports (eCA 2016a, b, e, f, g)

extraction. Chen et al. (2014) proposed an ionic liquid-based ultrasonic-assisted dispersive liquid–liquid microextraction method for highly effective extraction of trace bromadiolone and brodifacoum in environmental water samples.

Approaches such as QuEChERS (quick, easy, cheap, effective, rugged, and safe) appear to be suitable for the extraction of anticoagulant rodenticides from biological tissues such as aquatic organisms (Vudathala et al. 2010; Morrison et al. 2016). This approach generally relies on dispersive solid-phase extraction as a cleanup step after extraction to remove interferences from sample extracts. Several studies demonstrated that concurrently applying C_{18} and primary–secondary amine removes the majority of co-extracted materials by weight from moderately fatty fish tissue (Morrison et al. 2016). Besides mixed phase dispersive solid-phase extraction (Vudathala et al. 2010; Gómez-Canela and Lacorte 2016), gel-permeation chromatography (Hunter 1983b), normal phase solid-phase extraction using alumina or florisil cartridges (Jones 1996; Gómez-Canela and Lacorte 2016), and reversed phase solid-phase extraction using aminopropyl or hydrophilic-lipophilic balance cartridges (Goldade et al. 1998; Fisher et al. 2012; de Solla et al. 2016) were among the cleanup methods applied as an additional purification step to generate sample extracts suitable for quantitative analysis of anticoagulant rodenticides.

Qualitative and quantitative analysis

While coumatetralyl (hydroxycoumarin derivative) and chlorophacinone (indane-1,3-dione derivative) are well detectable by gas chromatography–mass spectrometry, gas chromatography-based methods have not proved reliable for the analysis of other anticoagulants because of either thermal degradation of the parent compound during chromatography, i.e., by heat of injection chamber, or insufficient derivatization (Hunter 1983a; Sato 2005). Hydroxycoumarin-based anticoagulant rodenticides are nonvolatile, highly adsorptive, and possess at least one functional hydroxyl group; thus, derivatization (with the exception of coumatetralyl) is required for their gas chromatography-based analysis (Sato 2005). Recently, an in-injector pyrolysis gas chromatograph coupled with an ion trap tandem mass spectrometer was shown to be successful for the rapid analysis of bromadiolone in blood plasma and liver without need for derivatization (Doubkova et al. 2017).

In general, analysis by liquid chromatography coupled with appropriate detectors, e.g., mass spectrometer or fluorescence detector, is the method of choice for detection of anticoagulant rodenticides in environmental samples following extraction and cleanup. Given the importance of primary and secondary poisoning, most methods are tailored toward the detection of specific active ingredients in various biological tissues of rodents, humans, domestic animals, and nontarget wildlife. A comprehensive summary of analytical methods for qualitative and quantitative determination of anticoagulant rodenticides in biological samples is also included in the work by Imran et al. (2015). As some of the compounds, e.g., brodifacoum and flocoumafen, are prone to carryover due to their nonpolar and hydrophobic nature (Marek and Koskinen 2007), extensive quality control is required irrespective of the chosen method to avoid false positives. Among the established methods for anticoagulant rodenticides in biological samples are ion-chromatography coupled with fluorescence detection (Jin et al. 2007) and tandem mass spectrometry (Jin et al. 2008), two-dimensional liquid chromatography coupled with tandem mass spectrometry (Marsalek et al. 2015), liquid chromatography coupled with tandem mass spectrometry (Marek and Koskinen 2007; Chen et al. 2009; Jin et al. 2009; Bidny et al. 2015), or high resolution mass spectrometry (Schaff and Montgomery 2013; Smith et al. 2017; Kotthoff et al. 2018). While anticoagulant rodenticides are suitable for electrospray ionization in both positive and negative mode, most published tandem and high resolution mass spectrometry methods rely on negative electrospray ionization due to enhanced sensitivity. A few researchers have employed atmospheric pressure chemical ionization on a limited number of anticoagulants (Guan et al. 1999;

Mandel et al. 2000). In addition, few methods employed direct injection of biological tissue extracts for the analysis of anticoagulants after solvent extraction without further cleanup (Bayen et al. 2015; Kotthoff et al. 2018). With regard to aqueous samples, sensitivity of nontarget screening methods employing minimal sample pretreatment, e.g., direct injection of aqueous samples or dilute-and-shoot approaches, might be insufficient for the detection of these compounds at very low ng/L concentrations.

Notably, none of these methods aimed at chromatographic separation of individual diastereoisomers. Core shell analytical columns or mobile phases containing acetonitrile were reported to separate anticoagulants into their different stereoisomers (Jones 1996; Fourel et al. 2017a), but chromatographic separation of all second-generation anticoagulant rodenticide stereoisomers within a single elution gradient is challenging (Damin-Pernik et al. 2016; Fourel et al. 2017a). After baseline separation of stereoisomers is achieved, peak acquisition of corresponding *cis*- and *trans*-isomers is usually carried out using identical multiple reaction monitoring settings in tandem mass spectrometry (Smith et al. 2017). A stereoselective method by Kammerer et al. (2005) determined phenprocoumon and its stereospecific metabolites based on liquid chromatography tandem mass spectrometry in positive electrospray ionization mode in human plasma and liver microsomes. In general, data on stereoisomer residues and their metabolites in rodents or nontarget wildlife after environmental exposure are limited (Damin-Pernik et al. 2016, 2017; Fourel et al. 2017a, b).

An overview of ions used for quantification and confirmation of anticoagulant rodenticides in various acquisition methods, i.e., selected ion monitoring, multiple reaction monitoring, and selected reaction monitoring, is provided elsewhere (Imran et al. 2015). Matrix- and compound-specific method detection limits (MDL) and method quantification limits (MQL) are discussed in the context of reported presence or absence of anticoagulants in the aquatic environment in subsequent sections.

Analytical challenges

The majority of studies that investigated the occurrence and fate of anticoagulant residues in the aquatic environment refrained from using adequate isotope labeled surrogates for individual compounds during analysis by liquid chromatography tandem mass spectrometry or high resolution mass spectrometry to account for incomplete extraction of bound residues, ion suppression, and matrix effects (Gómez-Canela et al. 2014a, b; Gómez-Canela and Lacorte 2016; Kotthoff et al. 2018). These days, isotopically labeled analogues of high purity can be purchased for the majority of anticoagulants. Although costly, the use of appropriate isotope labeled internal standards during analysis is highly recommended for the quantification of residues at trace levels in complex environmental samples to guarantee the required specificity and selectivity. Co-eluted matrix components can interfere and compete with ions of target analytes during ionization in samples with high protein and lipid content (Huerta et al. 2012). Internal standards can only correct for the variation in ionization efficiency if their behavior is similar to that of the target analytes. In case of warfarin, more pronounced matrix effects were observed in fish liver extracts compared to extracts derived from fillet tissue during liquid chromatography tandem mass spectrometry analysis (Ramirez et al. 2009). Moreover, findings by Ramirez et al. (2009) demonstrated that extracts derived from fish sampled at different locations exert variable influence on the analytical response of warfarin, even though extracts were derived from a single biological tissue. This is a major drawback for corrective measures such as matrix-matched external calibration or standard addition as the generation of a calibration curve for each sample is impractical and often omitted when analyzing large sample sets (Huerta et al. 2012).

Hence, reported concentrations of anticoagulant rodenticides in complex matrices should be examined carefully if their quantification was conducted by matrix-matched external standard calibration (Gómez-Canela and Lacorte 2016; Kotthoff et al. 2018) or by use of inappropriate internal standards, e.g., coumachlor as an internal standard for second-generation anticoagulant rodenticides (Gómez-Canela et al. 2014a, b). While physicochemical properties of coumachlor and the molecule's behavior in environmental matrices are similar to those of warfarin, they differ substantially from compounds such as bromadiolone, difenacoum, brodifacoum, difethialone, and flocoumafen (Table 2). In addition, the presence of coumachlor in environmental samples was demonstrated (Gómez-Canela and Lacorte 2016), precluding its qualification as an internal standard in regional monitoring studies. The range of target analytes as well as local conditions and emission sources plays an important role in choosing appropriate internal standards if labeled analogues are not available. Difenacoum for example has been commonly used as an internal standard for the quantification of brodifacoum in environmental samples collected from islands and fenced sanctuaries after aerial brodifacoum bait application (Masuda et al. 2015).

Chirality bears another challenge during residue analysis in complex matrices. Historically, chirality as a structural characteristic of pharmaceuticals marketed as racemates, e.g., vitamin K antagonists such as phenprocoumon, warfarin, and acenocoumarol, received very little attention in the field of environmental analysis (Pérez and Barceló 2008). Despite the fact that chromatographic separation of individual stereoisomers is of great value in pharmaco- and toxicokinetic studies

and offers new approaches for investigating their occurrence and fate in the environment, it adds another dimension of complexity to the screening of trace-level anticoagulant mixtures in environmental matrices. A major challenge for the quantitative assessment of individual stereoisomers in environmental samples is the lack of appropriate analytical standards and the non-disclosure of diastereoisomer ratios in biocidal products released to the environment.

Residues of anticoagulant rodenticides in terrestrial and avian nontarget species

Worldwide monitoring of anticoagulant residues focuses mainly on predators, e.g., UK (Walker et al. 2010), France (Lambert et al. 2007), Spain (López-Perea et al. 2015), USA (Murray 2011), New Zealand (Eason et al. 2002). Anticoagulant rodenticide residues are found in many birds of prey and owl species (Newton et al. 1990; Walker et al. 2008; Murray 2011; Christensen et al. 2012; Hughes et al. 2013). Here, mainly birds that prey on small mammals like common buzzards (*Buteo buteo*) (Berny et al. 1997; Laasko et al. 2010), red kites (*Milvus milvus*) (Laasko et al. 2010; Hughes et al. 2013; Coeurdassier et al. 2014), and barn owls (*Tyto alba*) (Hosea 2000; Lambert et al. 2007) are exposed to anticoagulant rodenticides. Furthermore, anticoagulant rodenticide residues regularly occur in mammalian predators like foxes (Berny et al. 1997; Beklova et al. 2007; Sage et al. 2010; Tosh et al. 2011; Sanchez-Barbudo et al. 2012), stoats, weasels, and polecats (McDonald et al. 1998; Shore et al. 2003). Beside ample data on the presence or absence of residues, some studies confirm (Jacquot et al. 2013) or suspect (Newton et al. 1997) population decreases in nontarget species due to anticoagulant rodenticide poisoning. Residues of mainly second-generation anticoagulant rodenticides were present in 60% of foxes (Geduhn et al. 2015) and 55% of barn owls (Geduhn et al. 2016) in Germany in 2011–2014, and density of farmland (livestock density) and urban areas was positively correlated to rodenticide exposure of foxes.

Anticoagulant rodenticide exposure of predators results from feeding on small mammals that are target or nontarget species of rodenticide applications. Few studies confirmed anticoagulant rodenticide residue occurrence in nontarget small mammals from European countries (Townsend et al. 1995; Brakes and Smith 2005; Tosh et al. 2012). In Germany, recent research demonstrated regular exposure to anticoagulant rodenticides in nontarget small mammals in a large-scale experimental study (Geduhn et al. 2014). 23% of individuals that were trapped in the surrounding of livestock farms where an anticoagulant rodenticide was applied showed anticoagulant residues in liver samples. Residues were found in all trapped small mammal species, including shrews and wood mice that are protected species in Germany. Exposure rates and residue concentrations were especially high close to the bait stations (15 m radius) and decreased with increasing distance to the baited area. Recently, the relevance of nontarget small mammals in the context of wildlife exposure to anticoagulants was demonstrated in mammals and owls (Geduhn et al. 2014, 2016). In Germany, barn owls regularly prey on nontarget small mammals and rarely on target mice or rats (Geduhn et al. 2016). Therefore, exposure of barn owls via nontarget small mammals is very likely. Furthermore, residues of anticoagulant rodenticides were detected in small mammals that were hunted by owls (Geduhn et al. 2016). The unacceptable risks of primary and secondary poisoning that has been identified within the authorization procedure of anticoagulant rodenticide under the Biocidal Product Regulation No. 528/2012 could be confirmed in different steps of the terrestrial food chain, with nontarget small mammals as a key factor in this process (Geduhn et al. 2014, 2015, 2016). Therefore, further efficient risk mitigation strategies are necessary that focus on these species to reduce overall wildlife exposure.

Occurrence and fate of anticoagulant rodenticides in the aquatic environment

Wastewater treatment plants

Despite the use of warfarin-containing baits by professional and private users in urban catchments, the presence of warfarin in raw and treated wastewater has mainly been linked to the consumption of blood-thinning medication by residents. While studies with radiolabeled warfarin in rabbits demonstrated that about 90% of the orally administered dose is recovered in urine (Wong and Solomonraj 1980), only about 2% of the typical 1–15 mg daily prescription dose is excreted as unchanged warfarin (Godfrey et al. 2007; Crouse et al. 2012). Urinary excretion of warfarin predominantly occurs in the form of metabolites as warfarin enantiomers are extensively metabolized by liver in mammals. While R warfarin is oxidized to 7-hydroxywarfarin and reduced to R,S warfarin alcohol, S warfarin (a more active enantiomer with 3–5 times higher anticoagulant potency) on the other hand is oxidized to 7-hydroxywarfarin and reduced to S,S warfarin alcohol. Both enantiomers can also be metabolized to 6-hydroxywarfarin (Kasprzyk-Hordern 2010).

The occurrence of more recalcitrant pharmaceuticals in wastewater treatment plants is often correlated with their prescription rates. The predicted national average concentration of warfarin in raw municipal wastewater, based on US marketing and pharmacological data from 2004, was estimated at 28 ng/L (Kostich and Lazorchak 2008). Very low warfarin concentrations, i.e., on average 2 ng/L, were measured in raw municipal wastewater influent at a wastewater

treatment plant facility in Texas, USA (Du et al. 2014). According to the authors, elevated concentrations of warfarin were occasionally observed in treated effluent, which might be explained by cleavage of glucuronide conjugates during biotransformation. Warfarin and its monohydroxylated derivatives are potential substrates for glucuronidation during phase II metabolism in humans. As glucoronide conjugates are more water-soluble than the parent compounds, they are easily excreted via bile and urine (Zielinska et al. 2008). Due to a rather high reporting limit of 11 ng/L, warfarin was not detected in wastewater effluent samples collected from 50 large wastewater treatment plants across the USA in 2011 (Kostich et al. 2014). It was sporadically detected in treated wastewater effluent used for irrigation from a facility in Colorado at levels up to 90 ng/L (Kinney et al. 2006).

In Finland, Ajo et al. (2018) reported warfarin concentrations of 82 ng/L and 7 ng/L in raw hospital wastewater and biologically treated domestic wastewater effluent from a healthcare center, respectively. Another study from Finland indicated better removal of warfarin (initial influent concentration of 50 ng/L) during membrane bioreactor treatment (more than 60% removal) compared to conventional activated sludge process (approximately 30% removal) (Gurung et al. 2016). The results of a study by Gibs et al. (2007) indicate that warfarin reacts completely with residual chlorine within 24 h during water treatment. Ejhed et al. (2018) investigated the treatment performance of three different onsite-wastewater treatment facilities that received raw wastewater collected from a small town in Germany (2500 person equivalents). Warfarin was only detected in one raw wastewater sample at 15 ng/L. It was not detected in any of the effluent samples (Ejhed et al. 2018). On the contrary, warfarin persisted in an organic-rich anoxic septic tank environment and was frequently detected in effluents from a community septic tank serving 350 users (Godfrey et al. 2007). Gómez-Canela et al. (2014b) detected warfarin in 9 out of 9 raw wastewater samples from wastewater treatment plants with mostly urban catchments in Catalonia, Spain. Warfarin concentrations in the aqueous phase of the 24-h composite samples ranged from 8 to 156 ng/L. It was also the main anticoagulant detected in more than 80 aqueous wastewater samples retrieved from nine wastewater treatment plants in Catalonia, Spain as 24-h composite samples in 2012 by the same research group. All samples were centrifuged prior to analysis, i.e., solid-phase extraction on hydrophilic-lipophilic balanced cartridges followed by liquid chromatography tandem mass spectrometry, to remove particulate matter. Warfarin concentrations ranged from 9 to 334 ng/L in raw wastewater and 1.6–45 ng/L in biologically treated wastewater effluents, respectively. Highest warfarin concentrations were detected in facilities serving large urban catchment areas. The majority of the studied wastewater treatment plants removed warfarin to below its method detection limit (MDL) of 1.6 ng/L in treated effluents. Three other facilities achieved removal rates between 82% and 98% (Gómez-Canela et al. 2014a). Santos et al. (2013) detected warfarin in hospital and municipal effluents in Portugal in the low ng/L range, supporting the hypothesis that the presence of warfarin in wastewater is mainly caused by its use as pharmaceutical.

Gómez-Canela et al. (2014a) also reported sporadic occurrence of coumatetralyl, difenacoum, bromadiolone, flocoumafen, and brodifacoum in wastewater samples, but failed in establishing meaningful input and elimination routes. Although most of the investigated wastewater treatment plants indicated high anticoagulant rodenticide removal efficiencies from the aqueous compartment, traces of anticoagulants remained in the treated effluent and were likely discharged into receiving surface waters (Gómez-Canela et al. 2014a). In another study by the same research group, Gómez-Canela and Lacorte (2016) detected anticoagulant rodenticides in sludge intended to be used as agricultural fertilizer at 15 out of 27 investigated wastewater treatment plants across North-East Spain. Of all analyzed anticoagulant rodenticides, warfarin was detected most frequently in the low µg/kg range based on dry weight. Bromadiolone was detected in sludge samples from six treatment facilities at concentrations between 5 and 8 µg/kg. Brodifacoum occurred in two sludge samples at 15 µg/kg and 17 µg/kg levels, respectively. Difenacoum and flocoumafen were not detected in any of the sludge samples. It was concluded that anticoagulant rodenticides enter wastewater treatment plants as a result of their use as pest control in urban infrastructures, domestic applications, as pharmaceuticals, or in agriculture (Gómez-Canela et al. 2014a, b; Gómez-Canela and Lacorte 2016).

In 2008, Sweden performed a national screening program to determine concentrations of chlorophacinone, coumatetralyl, difenacoum, brodifacoum, bromadiolone, and flocoumafen in the Swedish environment. None of the analyzed anticoagulant rodenticides was detected above their respective MDL of 5 ng/L and 1 µg/kg in several raw and treated wastewater as well as sludge samples (Norström et al. 2009).

Surface water, stormwater runoff, and groundwater

A surface water monitoring campaign in Lower Saxony, Germany in 2014 included the analytes warfarin, bromadiolone, and difenacoum. None of the three were detected in aqueous samples from surface waters above their method quantification limit (MQL) of 5 ng/L (Steffen 2014). Chen et al. (2014) analyzed bromadiolone and brodifacoum in environmental water samples from streams and groundwater wells in China. With one exception, both target analytes were below their respective MQL in all analyzed samples (0.22 µm membrane filtered). Brodifacoum was detected in one surface water sample at 0.56 µg/L and was traced

back to illegal untreated wastewater discharges from a production facility into the stream (Chen et al. 2014). Brodifacoum was also detected in one organic-rich freshwater sample at 0.48 µg/L several days after aerially broadcasted application of bait pellets (approximately 39 metric tons of bait with 0.975 kg active ingredient distributed across 2.5 km^2) during island eradication (Pitt et al. 2015). Chlorophacinone and bromadiolone were not detectable in groundwater samples from open space in Spain after bait application to eradicate country vole (Hernández et al. 2013). Screening of water samples collected from a freshwater lake in New Zealand (approximately 0.3 km^2 surface area, 10–40 m depth) after accidental discharge of 700 kg of brodifacoum containing bait pellets (14 g of active ingredient) revealed no detects of residual brodifacoum in the month after the spill (Fisher et al. 2012). None of the analyzed six anticoagulant rodenticides were detected in Swedish surface water and stormwater runoff samples above the MDL of 5 ng/L (Norström et al. 2009).

During several nationwide US groundwater and surface water monitoring campaigns, warfarin was not detected above its reporting limit of 1 ng/L in any of the analyzed samples (Kolpin et al. 2002, 2004; Barnes et al. 2008; Focazio et al. 2008). However, Watkins et al. (2014) detected warfarin in surface water samples collected from suburban streams in Houston, Texas at locations downstream of wastewater treatment plant discharges. Reported concentrations ranged between 1 and 13 ng/L. Warfarin was not detected above its MDL of 0.8 ng/L in samples collected from locations upstream of discharges. Owing to a very high MDL of 50 ng/L, warfarin was also not detected in more than 1200 groundwater samples from California (Fram and Belitz 2011). Furthermore, warfarin showed significant attenuation during soil aquifer treatment of septic tank effluents. The passage of effluent through 2 m of a partially saturated, sand-dominated vadose zone reduced warfarin concentrations to below MDL in groundwater samples collected from an adjacent well. Attenuation processes were most likely a combination of sorption to the porous media and microbial degradation (Godfrey et al. 2007).

Interestingly, only one study by Wode et al. (2015) investigated the occurrence of phenprocoumon, an anticoagulant that is predominantly administered across Europe, in surface water and groundwater samples affected by treated wastewater effluents using a liquid chromatography high resolution mass spectrometry target screening approach. Phenprocoumon was qualitatively detected in 7 out of 14 groundwater and 7 out of 11 surface water samples of a former wastewater infiltration site in Berlin, Germany. As discussed earlier, estimated prescribed doses of phenprocoumon in Germany in 2016 exceeded those of warfarin by a factor of 40. Other than warfarin, phenprocoumon is excreted almost entirely as a glucuronide conjugate, with less than 10% of the dose as unchanged drug (Kasprzyk-Hordern 2010).

Soils and sediments

Kinney et al. (2006) assessed the presence and distribution of warfarin in soil irrigated with reclaimed water derived from urban wastewater. Warfarin did not accumulate in the studied soils over time and was present in the soils as low percentage of the mass applied. Observed concentration differences within the soil profiles may indicate the potential for warfarin to be transported from the soil surface to groundwater (Kinney et al. 2006). Residual flocoumafen was confirmed in two out of 21 New Zealand estuarine sediment samples. None of the monitored anticoagulant rodenticides were detected at riverine sites (Cavanagh and Ward 2014). After the accidental spill of brodifacoum containing bait into a freshwater lake in New Zealand, surface layer sediment samples revealed no detects of residual brodifacoum (Fisher et al. 2012). Nevertheless, 32% of soil samples from areas affected by broadcasted application of pellet bait contained brodifacoum residues at levels up to 56 µg/kg (MDL 3 µg/kg) (Pitt et al. 2015). Soil and sediment samples (upper 2–3 cm layer) from urban and remote areas in Sweden contained no traces of anticoagulant rodenticide residues (Norström et al. 2009).

Suspended particulate matter

Suspended particulate matter samples from the German Specimen Bank were analyzed by Kotthoff et al. (2018) using liquid chromatography high resolution mass spectrometry to assess residue levels and distribution patterns of anticoagulant rodenticides in German surface waters. Samples, i.e., pooled samples of 12 monthly subsamples, were collected in 2015 from 16 different streams according to standardized procedures and corresponded with sampling sites of investigated limnic fish. Bromadiolone was the only anticoagulant rodenticide detected above its MQL of 1 µg/kg in nine suspended particulate matter samples and deviated from fish liver results discussed in the following. Mean concentration of bromadiolone was 4.9 µg/kg with a maximum of 9.2 µg/kg. The rather unexpected absence of other anticoagulant rodenticides in suspended particulate matter samples remained unresolved (Kotthoff et al. 2018).

Aquatic organisms

Liver samples of bream (*Abramis brama*) analyzed in the same study were also obtained from the German Specimen Bank (Kotthoff et al. 2018). Samples were collected in 2011 and 2015 and represented 16 river sampling sites

and two lakes across Germany. In addition, decennial time series were analyzed for two sampling locations, i.e., rivers Saar and Elbe. According to their findings, five out of eight authorized anticoagulant rodenticides, namely difenacoum, brodifacoum, bromadiolone, difethialone, and flocoumafen, were detected in fish liver samples above their respective MQL of 0.2–2.0 µg/kg wet weight. In several fish liver samples, more than one residue was detected. This is in accordance with studies investigating anticoagulant rodenticide exposure in terrestrial nontarget wildlife. Different substance and concentration patterns were found between 2011 and 2015. Notably, brodifacoum was detected in 88% of the 2015 samples with an average concentration of 3.4 µg/kg (max. 12.5 µg/kg), followed by difenacoum (44%, max. 0.7 µg/kg) and bromadiolone (17%, max. 7.1 µg/kg). Metabolism and depuration of bromadiolone in fish might have caused the varying detection frequencies of bromadiolone residues in corresponding samples of fish liver (19%) and suspended particulate matter (56%) (Kotthoff et al. 2018). In a New Zealand study from 2013, a total of 49 individual freshwater fish livers, among others from brown trout (*Salmo trutta*) and New Zealand longfin eel (*Anguilla dieffenbachii*), were screened for residues of warfarin (MDL 100 µg/kg), coumatetralyl (MDL 10 µg/kg), brodifacoum, bromadiolone, and flocoumafen (all MDL 5 µg/kg). About 27% of analyzed liver samples contained bromadiolone (9–34 µg/kg wet weight) or coumatetralyl (11–24 µg/kg wet weight), respectively. Residues were not detected above their respective MDL in corresponding muscle tissue samples (Cavanagh and Ward 2014).

Warfarin was sporadically detected in tissues of wild freshwater mussels (*Lasmigona costata*) collected in 2012 from the Grand River, Ontario in Canada, but not in a series of corresponding surface water samples (2009–2011, $n=37$). The reported maximum tissue concentration of warfarin was 1.15 µg/kg wet weight. Warfarin was not detected above its MDL in tissues of caged freshwater mussels after a 4-week deployment period in Grand River in 2010 (de Solla et al. 2016). Warfarin was also not detected in any of the fish fillet (MDL 0.9 µg/kg, $n=30$) or liver (MDL 2.7 µg/kg, $n=30$) composite samples from five effluent-dominated river sampling sites receiving discharge from wastewater treatment plants of major cities across the USA (Ramirez et al. 2009). The 2008 Swedish national screening program included fish muscle samples (pooled samples of hering and perch, respectively) from remote and urban surface waters to investigate the occurrence of chlorophacinone, coumatetralyl, difenacoum, brodifacoum, bromadiolone, and flocoumafen in the Swedish environment. Their concentrations were below the MDL of 1 µg/kg in all fish muscle samples (Norström et al. 2009).

Other findings in aquatic organisms include (sparse) residual concentrations of brodifacoum in coastal marine species such as sedentary mollusks and fish following island rodent eradication (Siers et al. 2016) or accidental discharge (Primus et al. 2005). Residual brodifacoum concentrations were found in liver samples, but not muscle tissue, of two blue cod (*Parapercis colias*) individuals at 26 µg/kg and 92 µg/kg, respectively (8% detection frequency). Brodifacoum residues were also detected in whole-body samples of four mussels (*Mytilus edulis*) in the range of 1–22 µg/kg and four limpets (*Cellana ornata*) in the range of 1–16 µg/kg (17% detection frequency) (Masuda et al. 2015). Following a hand- and aerially broadcast application of 18,000 kg of brodifacoum pellets on Wake Island Atoll in 2012, 3 out of 69 marine whole-body fish samples collected in 2012 and 5 out of 48 collected in 2015 were suspected of brodifacoum contamination (MDL 3.5 µg/kg). However, none of these whole-body samples (mostly from blacktail snappers, *Lutjanus fulvus*) yielded reliably quantifiable concentrations of brodifacoum above the MQL of 11.7 µg/kg (Siers et al. 2016). Pitt et al. (2015) conducted a comprehensive post-baiting monitoring for environmental brodifacoum residues after the extensive rat eradication on Palmyra Atoll. Whole-body samples of black-spot sergeants (*Abudefduf sordidus*) that were collected prior to baiting contained no brodifacoum residues above the MDL of 13 µg/kg, whereas average brodifacoum concentrations were in the range of 143 ± 27 µg/kg (90% detection frequency) shortly after aerially broadcasted bait application (approximately 0.39 mg active ingredient per m^2 land surface). The mortality of 47 mullets (*Moolgarda engeli, Liza vaigiensis*) washed ashore was linked to brodifacoum bait application. Whole-body samples showed average residues of 337 ± 67 µg/kg wet weight. As mullets are common prey of many aquatic and terrestrial predatory species, the authors emphasized the likeliness of trophic transfer of brodifacoum (Pitt et al. 2015). According to a literature review by Masuda et al. (2015), detection frequencies of brodifacoum residue in coastal marine species after aerial bait application were only approximately 6% for marine invertebrates and 3% for fish. No residual brodifacoum was detected in fish liver samples (*Anguilla diefenbachii*) after accidental discharge of 14 g of active ingredient into a remote freshwater lake in New Zealand (Fisher et al. 2012). Green mussel (*Perna viridis*) samples collected in Singapore coastal waters showed no traces of warfarin above its MDL of 0.6 µg/kg wet weight (Bayen et al. 2015).

Avian and mammalian predators in the aquatic food web

Liver samples of different top-predator species with a predominantly fish-eating diet across the Loire river basin in France were screened for residues of warfarin, chlorophacinone, coumatetralyl, difenacoum, brodifacoum,

bromadiolone, difethialone, and flocoumafen by Lemarchand et al. (2014). Carcasses of road-traffic killed Eurasian otter were mainly collected between 2004 and 2008 (Lemarchand et al. 2010). While samples of great cormorants (*Phalacrocorax carbo carbo/sinensis*) and osprey (*Pandion haliaetus*) revealed no traces of anticoagulants above their respective MDL of 20 µg/kg, bromadiolone was detected in 10% of the analyzed 20 Eurasian otter (*Lutra lutra*) liver samples at concentrations of 0.4 and 0.85 mg/kg wet weight, respectively. No clinical signs of intoxication, e.g., severe anemia or bleeding, were observed. As both individuals originated from the same riparian area that was heavily baited against proliferation of land voles (*Arvicola scherman*) back then, the authors deemed secondary poisoning due to predation on nontarget rodents likely (Lemarchand et al. 2010; Lemarchand et al. 2014). An earlier study by Fournier-Chambrillon et al. (2004) confirmed exposure of European otters to secondary poisoning by bromadiolone (18%) and chlorophacinone (9%) in France due to major field treatments with anticoagulants in the past. Hepatic traces of coumatetralyl (5.8–9.4 µg/kg), bromadiolone (6.2–11 µg/kg), and difenacoum (lower than 0.3–2.5 µg/kg) were also found in two roadkill European otters from Finland (Koivisto et al. 2016). No anticoagulant rodenticides were detected above their respective MQL of 0.2–2.0 µg/kg in liver samples of five European otter individuals from the river Elbe catchment in Eastern Germany (Kotthoff et al. 2018).

Following aerial rodent eradication in 2009, three out of nine little blue penguins (*Eudyptula minor*) found dead on island beaches showed hepatic brodifacoum residues (Fisher 2013). As a consequence, a more comprehensive screening of liver samples from 38 penguin carcasses regarding brodifacoum, bromadiolone, flocoumafen, coumatetralyl, and warfarin residues was conducted in 2010. While target analytes were absent in 50% of the penguin liver samples, 34.2% revealed the presence of one anticoagulant, 7.9% a combination of two, 5.3% of three and 2.6% of four different anticoagulants. Brodifacoum was detected in six of the little blue penguins in the range of 1–3 µg/kg (Fisher 2013).

Rating the risks of anticoagulant rodenticides in the aquatic environment

Challenges of anticoagulant rodenticide residue screening in aquatic environmental compartments

Monitoring of anticoagulant rodenticide residues in the aquatic environment involves a number of challenges, particularly with regard to establishing causative associations and robust source, pathway, and receptor relationships. Given the toxicological relevance of anticoagulants at trace concentrations and the variety of active ingredients applied worldwide, very sensitive and specific multi-methods are required that cover a wide range of different compounds and environmental matrices. As illustrated in this review, available analytical methods often suffer from elevated limits of detection caused by the complexity of environmental matrices such as sewage or biological tissues and insufficient sample pretreatment.

Another critical consideration in the context of poisoning via environmental emissions is the influence of municipal effluent discharges on in-stream hydrology when selecting sampling locations and periods for monitoring of wastewater-derived contaminant exposure (Ramirez et al. 2009). Important aspects regarding the monitoring of anticoagulant rodenticides in aquatic compartments are the frequency and amplitude of contaminant loadings. Effluent-dominated systems generally represent worstcase exposure scenarios, but it is assumed that anticoagulant rodenticide input rates are of transient character and will vary widely depending on usage patterns in urban catchments, runoff regimes, and wastewater treatment plant performance. Worstcase predicted environmental concentrations discussed earlier (Table 1) indicate that expected anticoagulant rodenticide concentrations in receiving surface waters may be out of reach for current analytical methods, even with extensive sample enrichment and cleanup. Yet, in cases where environmental dissipation rates are exceeded by prolonged input rates from effluent loadings, even at very low concentrations, effective exposure duration of organisms residing in these aquatic systems is increased, presenting particular potential for accumulation of contaminants. Thus, analysis of stationary environmental matrices such as sediments, sessile or less migratory organisms that reflect an average exposure over time can be one way to capture transient events and monitor the burden of the aquatic environment (Kotthoff et al. 2018). Bioaccumulation processes can widely differ among aquatic species due to complex interactions between various routes of uptake (aqueous uptake of water-borne chemicals, dietary uptake by ingestion of contaminated food or particles), excretion, passive release, and metabolization (Streit 1998). Therefore, determination of concomitant parameters such as trophic level, age, and lipid content is crucial to rank the exposure of aquatic organisms and link anticoagulant rodenticide residues to identified emission sources. Yet, such important parameters were often omitted in environmental monitoring studies of anticoagulants in aquatic wildlife. The occurrence and fate of anticoagulant rodenticides in fish species is likely correlated with their feeding habit and lipid metabolism, i.e., less fat after winter months. In summer and fall, lipid content in fish is usually highest and river water levels lowest, e.g., less dilution of wastewater-derived contaminants.

Emergence of anticoagulants in the aquatic environment

With the exception of warfarin, behavior and fate of anticoagulant rodenticides in the aquatic environment have received minimal attention by environmental research groups in the past. Therefore, potential risks cannot be adequately rated at this point. Several studies considered the risk of secondary poisoning via environmental emissions as marginal. The Swedish monitoring study concluded that anticoagulant rodenticides are not widely distributed in the Swedish environment, thus not posing a threat for nontarget organisms that are not affected by direct primary or secondary poisoning (Norström et al. 2009). Nonetheless, this review clearly shows that anticoagulant rodenticides can enter aquatic environmental compartments. Without question, more comprehensive monitoring data of relevant environmental matrices are needed for a thorough assessment of their emergence. Given their physicochemical properties (Table 2), environmental matrices such as sediments and suspended particulate matter might pose important exposure routes for particle-bound second-generation anticoagulant rodenticides, leading to bioaccumulation and toxicity in aquatic organisms. According to Fisher (2013), environmental spread of anticoagulant rodenticide residues in New Zealand is thought to be predominantly trophic rather than through exposure of nontarget organisms to anticoagulant rodenticide residues in water or soil/sediments. Carcasses of poisoned animals or terrestrial invertebrates that feed on bait, e.g., cockroaches, are presumed to transfer anticoagulant rodenticide residues in the aquatic environment and put predators and scavengers at risk of secondary exposure.

Warfarin is commonly monitored in environmental studies because of its substantial volume of prescriptions and sales, alongside its potential negative effects on wildlife. In developed countries, the occurrence of warfarin in the aquatic environment is mainly caused by its use as a prescription drug and incomplete removal (or reversible transformation) during conventional wastewater treatment. Low detection frequencies of warfarin in the aquatic environment are likely a combination of low consumption compared to other high-volume non-prescription drugs, high metabolic rates in the body of humans (pharmaceutical) and rodents (biocidal use), low bioaccumulation potential, and high detection limits. In surface water and groundwater, warfarin reporting limits differed by factor 50 among studies, ranging between 0.001 µg/L (Kolpin et al. 2002, 2004; Barnes et al. 2008; Focazio et al. 2008) and 0.05 µg/L (Fram and Belitz 2011; Crouse et al. 2012). The worstcase predicted environmental concentrations for surface water resulting from sewer baiting scenarios are in the range of 0.006 µg/L (Table 1). According to reviewed monitoring data, environmental levels of warfarin may not represent a high risk for aquatic species, in particular fish and mollusks. Moreover, warfarin was not ranked as an emerging contaminant in coastal and marine environments (Maruya et al. 2015). Yet, chronic exposure at low concentrations or chronic exposure with multiple active ingredients and therefore higher environmental concentrations could trigger sublethal effects (Fernandez et al. 2014).

Future research needs and risk mitigation measures

The proposed adverse outcome pathway for anticoagulant rodenticides in terrestrial nontarget wildlife by Rattner et al. (2014) reveals that the anticoagulant's mechanism of action from the molecular through cellular levels is well understood, whereas linkages and forecasting of responses at the individual through population levels remain vague or incomplete. Among others, substantial data gaps exist regarding the understanding of exposure pathways and potential adverse effects of multiple low-level anticoagulant rodenticide exposures. For instance, the almost ubiquitous occurrence of second-generation anticoagulant rodenticides in bream liver samples from receiving surface waters throughout Germany demonstrated by Kotthoff et al. (2018) contrasts the reported (minor) quantities of active ingredients applied as biocides in German sewer systems (Krüger and Solas 2010). Notably, rodent control in sewer systems is one of the main applications of biocidal anticoagulant rodenticides in densely populated urban and peri-urban areas in Germany. At present, studies about the fate of anticoagulant rodenticide residues during wastewater treatment, e.g., conventional or advanced treatment, respectively, after confirmed bait application in sewer systems of urban catchments are lacking.

The role of invertebrates as consumers and vectors of anticoagulant poison should be another research priority in the context of anticoagulant rodenticide spread in the aquatic environment. American cockroaches (*Periplaneta americana*), which can be widely distributed among sewer manholes, demonstrated an ability to consume an entire anticoagulant rodenticide bait placement (Colvin et al. 1998). Although anticoagulants are unlikely to affect invertebrates in the same way as vertebrates because of fundamental differences in the blood clotting system, vertebrates that prey on invertebrates can be affected by secondary poisoning. Terrestrial invertebrates can be an important component of stream fish diets, especially during the summer months, when aquatic invertebrates are limited (Garman 1991). Cockroaches can be available as fish prey when swept into the water column. Pitt et al. (2015) demonstrated in their study that brodifacoum residue levels in cockroaches were consistently the highest among the biological samples

collected. In New Zealand, residues of brodifacoum were also detected in the tissues of cave weta (*Rhaphidophoridae* sp.) that were found on baits (Ogilvie et al. 1997).

Moreover, the understanding of mechanistic relationships between bioaccumulation and toxicity of anticoagulant rodenticides demands further improvement, e.g., by incorporation in toxicokinetic and toxicodynamic modeling. While detection of hepatic anticoagulant rodenticide residues in aquatic organisms should not be dismissed, sole consideration of these findings and the implied potential biomagnification along the aquatic food chain is insufficient with regard to a profound anticoagulant rodenticide risk assessment. Instead, bioaccumulation of anticoagulant rodenticides should be linked to adverse effects and relative potencies on each trophic level so that risks can be evaluated for specific target species along the food web, e.g., invertebrates, fish, or top predators. In the terrestrial food chain, risk via poisoned rodents is considered significantly higher compared to risk via earthworms or other invertebrates (eCA 2016g). To mitigate the risk of secondary exposure, however, first-generation anticoagulant rodenticides and less potent second-generation anticoagulant rodenticides should always be considered as the first choice for pest control with anticoagulants.

Conclusion

Recent findings of anticoagulant rodenticides in the aquatic food web as discussed in this review demonstrate that the aquatic environment experiences a greater risk of anticoagulant exposure than previously thought. Besides the discussed analytical challenges, knowledge gaps and the lack of detailed market data clearly hamper the establishment of resilient exposure pathways with regard to the aquatic environment. Beyond doubt, more comprehensive monitoring data are required for all anticoagulants in the aquatic environment to establish robust relationships and causative associations as previously demonstrated for the unintended poisoning of terrestrial nontarget organisms. Once those are established, more effective and practical risk mitigation measures, e.g., alternatives to anticoagulant rodenticides for rodent control in sewer systems, can be proposed, implemented, and their sustained success reassessed.

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References

Ajo P, Preis S, Vornamo T, Mänttäri M, Kallioinen M, Louhi-Kultanen M (2018) Hospital wastewater treatment with pilot-scale pulsed corona discharge for removal of pharmaceutical residues. J Environ Chem Eng 6:1569–1577. https://doi.org/10.1016/j.jece.2018.02.007

Alomar H, Chabert A, Coeurdassier M, Vey D, Berny P (2018) Accumulation of anticoagulant rodenticides (chlorophacinone, bromadiolone and brodifacoum) in a non-target invertebrate, the slug, Deroceras reticulatum. Sci Total Environ 610–611:576–582. https://doi.org/10.1016/j.scitotenv.2017.08.117

Andre C, Guyon C, Guillaume YC (2004) Rodenticide-humic acid adsorption mechanisms and role of humic acid on their toxicity on human keratinocytes: chromatographic approach to support the biological data. J Chromatogr, B: Anal Technol Biomed Life Sci 813:295–302. https://doi.org/10.1016/j.jchromb.2004.10.028

Andre C, Guyon C, Thomassin M, Barbier A, Richert L, Guillaume YC (2005) Association mechanism between a series of rodenticide and humic acid: a frontal analysis to support the biological data. J Chromatogr, B: Anal Technol Biomed Life Sci 820:9–14. https://doi.org/10.1016/j.jchromb.2005.02.020

Barnes KK, Kolpin DW, Furlong ET, Zaugg SD, Meyer MT, Barber LB (2008) A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States - I) groundwater. Sci Total Environ 402:192–200. https://doi.org/10.1016/j.scitotenv.2008.04.028

Barten R (2014) New approaches from the view of industry. In: Esther A et al (eds) Rodenticide resistance. Julius Kühn Institute, Federal Research Centre for Cultivated Plants, Braunschweig, pp 50–54

Battersby SA (2015) Rodents as carriers of disease. In: Buckle AP, Smith RH (eds) Rodent pests and their control. CABI, Oxfordshire, pp 81–100

Bayen S, Estrada ES, Juhel G, Kelly BC (2015) Direct injection of tissue extracts in liquid chromatography/tandem mass spectrometry for the determination of pharmaceuticals and other contaminants of emerging concern in mollusks. Anal Bioanal Chem 407:5553–5558. https://doi.org/10.1007/s00216-015-8760-9)

Beklova M, Krizkova S, Supalkova V et al (2007) Determination of bromadiolone in pheasants and foxes by differential pulse voltammetry. Int J Environ Anal Chem 87:459–469. https://doi.org/10.1080/03067310601170472

Berny PJ, Buronfosse T, Buronfosse F, Lamarque F, Lorgue G (1997) Field evidence of secondary poisoning of foxes (Vulpes vulpes) and buzzards (Buteo buteo) by bromadiolone, a 4-year survey. Chemosphere 35:1817–1829. https://doi.org/10.1016/S0045-6535(97)00242-7

Berny P, Velardo J, Pulce C, D'Amico A, Kammerer M, Lasseur R (2010) Prevalence of anticoagulant rodenticide poisoning in humans and animals in France and substances involved. Clin Toxicol (Phila) 48:935–941. https://doi.org/10.3109/15563650.2010.533678

Bidny S, Gago K, David M, Duong T, Albertyn D, Gunja N (2015) A validated LC-MS-MS method for simultaneous identification and quantitation of rodenticides in blood. J Anal Toxicol 39:219–224. https://doi.org/10.1093/jat/bku175

Booth LH, Ogilvie SC, Eason CT (2010) Persistence of sodium monofluoroacetate (1080), pindone, cholecalciferol, and brodifacoum in possum baits under simulated rainfall. N Z J Agric Res 42:107–112. https://doi.org/10.1080/00288233.1999.9513359

Brakes CR, Smith RH (2005) Exposure of non-target small mammals to rodenticides: short-term effects, recovery and implications for secondary poisoning. J Appl Ecol 42:118–128. https://doi.org/10.1111/j.1365-2664.2005.00997.x

Buckle AP, Eason CT (2015) Control methods: chemical. In: Buckle AP, Smith RH (eds) Rodent pests and their control. CAB International, Wallingford, pp 123–154

Buckle AP, Smith RH (eds) (2015) rodent pests and their control. CAB International, Wallingford
BVL (2012) Absatz an Pflanzenschutzmitteln in der Bundesrepublik Deutschland. Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Braunschweig
BVL (2015) Absatz an Pflanzenschutzmitteln in der Bundesrepublik Deutschland. Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Braunschweig
Cavanagh J-AE, Ward N (2014) Contaminants in estuarine and riverine sediments and biota in Southland. Environment Southland, Invercargill
Chen XH, Cai MQ, Ouyang XK, Jin MC (2009) Ion chromatography tandem mass spectrometry for simultaneous confirmation and determination of indandione rodenticides in serum. Biomed Chromatogr 23:1217–1226. https://doi.org/10.1002/bmc.1246
Chen M, Zhu G, Zhou L, Min J, Chen X, Jin M (2014) Analysis of trace bromadiolone and brodifacoum in environmental water samples by ionic liquid ultrasound-assisted dispersive liquid–liquid microextraction and LC-MS/MS. Anal Methods 6:5879–5885. https://doi.org/10.1039/c3ay42317d
Christensen TK, Lassen P, Elmeros M (2012) High exposure rates of anticoagulant rodenticides in predatory bird species in intensively managed landscapes in Denmark. Arch Environ Contam Toxicol 63:437–444. https://doi.org/10.1007/s00244-012-9771-6
Coeurdassier M, Riols R, Decors A et al (2014) Unintentional wildlife poisoning and proposals for sustainable management of rodents. Conserv Biol 28:315–321. https://doi.org/10.1111/cobi.12230
Colvin BA, Swift TB, Fothergill FE (1998) Control of Norway rats in sewer and utility systems using pulsed baiting methods. In: Proceedings of the 18th vertebrate pest conference, vol 36, pp 247–253
Connors KA, Du B, Fitzsimmons PN et al (2013) Comparative pharmaceutical metabolism by rainbow trout (Oncorhynchus mykiss) liver S9 fractions. Environ Toxicol Chem 32:1810–1818. https://doi.org/10.1002/etc.2240
Crouse BA, Ghoshdastidar AJ, Tong AZ (2012) The presence of acidic and neutral drugs in treated sewage effluents and receiving waters in the Cornwallis and Annapolis River watersheds and the Mill CoveSewage Treatment Plant in Nova Scotia, Canada. Environ Res 112:92–99. https://doi.org/10.1016/j.envres.2011.11.011
CRRU UK (2015) Campaign for responsible rodenticide Use UK code of best practice. Campaign for Responsible Rodenticide Use UK, Leeds
Damin-Pernik M, Espana B, Besse S et al (2016) Development of an ecofriendly anticoagulant rodenticide based on the stereochemistry of difenacoum. Drug Metab Dispos 44:1872–1880. https://doi.org/10.1124/dmd.116.071688
Damin-Pernik M, Espana B, Lefebvre S et al (2017) Management of rodent populations by anticoagulant rodenticides: toward third-generation anticoagulant rodenticides. Drug Metab Dispos 45:160–165. https://doi.org/10.1124/dmd.116.073791
Dawson A, Garthwaite D (2004) Rodenticide usage by local authorities in Great Britain 2001. Pesticide usage survey report 185. Department for Environment, Food and Rural Affairs, New York
de Solla SR, Gilroy EA, Klinck JS et al (2016) Bioaccumulation of pharmaceuticals and personal care products in the unionid mussel Lasmigona costata in a river receiving wastewater effluent. Chemosphere 146:486–496. https://doi.org/10.1016/j.chemosphere.2015.12.022
Doubkova V, Marsalek P, Vecerek V (2017) The rapid determination of bromadiolone in liver and blood plasma by in-injector pyrolysis gas chromatography—ion trap tandem mass spectrometry. J Chromatogr, B: Anal Technol Biomed Life Sci. https://doi.org/10.1016/j.jchromb.2017.10.027
Du B, Price AE, Scott WC et al (2014) Comparison of contaminants of emerging concern removal, discharge, and water quality hazards among centralized and on-site wastewater treatment system effluents receiving common wastewater influent. Sci Total Environ 466–467:976–984. https://doi.org/10.1016/j.scitotenv.2013.07.126
Eason CT, Murphy EC, Wright GR, Spurr EB (2002) Assessment of risks of brodifacoum to non-target birds and mammals in New Zealand. Ecotoxicol 11:35–48. https://doi.org/10.1023/A:1013793029831
EBPF (2015) Sustainable use of rodenticides as biocides in the EU. CEFIC-European Biocidal Products Forum, Brussels
eCA (2016a) Flocoumafen assessment report. Product-type 14 (Rodenticide) competent authority. European Union, The Netherlands
eCA (2016b) Coumatetralyl assessment report. Product-type 14 (Rodenticide) competent authority. European Union, Denmark
eCA (2016c) Brodifacoum assessment report. Product-type 14 (Rodenticide) competent authorities. European Union, The Netherlands and Italy
eCA (2016d) Chlorophacinone assessment report. Product-type 14 (Rodenticide) competent authority. European Union, Spain
eCA (2016e) Bromadiolone assessment report. Product-type 14 (Rodenticide) competent authority. European Union, Italy
eCA (2016f) Warfarin Assessment report. Product-type 14 (Rodenticide) competent authority. European Union, Ireland
eCA (2016g) Difenacoum assessment report. Product-type 14 (rodenticide) competent authority. European Union, Finland
eCA (2016h) Difethialone assessment report. Product-type 14 (Rodenticide) competent authority. European Union, Norway
ECHA (2017a) Guidance on the biocidal products regulation: volume IV environment—assessment and evaluation (parts B + C). European Chemicals Agency, Helsinki
ECHA (2017b) Opinion of the Biocidal Products Committee on questions related to the comparative assessment of anticoagulant rodenticides. ECHA/BPC/145/2017. European Chemicals Agency, Helsinki
Ejhed H, Fang J, Hansen K et al (2018) The effect of hydraulic retention time in onsite wastewater treatment and removal of pharmaceuticals, hormones and phenolic utility substances. Sci Total Environ 618:250–261. https://doi.org/10.1016/j.scitotenv.2017.11.011
Elliott JE, Rattner BA, Shore RF, Van Den Brink NW (2016) Paying the pipers: mitigating the impact of anticoagulant rodenticides on predators and scavengers. Biosci 66:401–407. https://doi.org/10.1093/biosci/biw028
Empson RA, Miskelly CM (1999) The risks, costs and benefits of using brodifacoum to eradicate rats from Kapiti Island, New Zealand. N Z J Ecol 23:241–254
Endepols S (2002) Rodenticides—indispensable for safe food production. Pestic Outlook 13:231–232. https://doi.org/10.1039/b211694b
European Commission (2011) Regulation (EU) No 253/2011 of 15 March 2011 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annex XIII. Off J Eur Union L 69:7–12
European Commission (2016) Commission Regulation (EU) 2016/1179 of 19 July 2016 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures. Off J Eur Union L 195:11–25
European Commission (2017a) Commission Implementing Regulation (EU) 2017/1380 of 25 July 2017 renewing the approval of bromadiolone as an active substance for use in biocidal products of product-type 14. Off J Eur Union L 194:33–38
European Commission (2017b) Commission Implementing Regulation (EU) 2017/1379 of 25 July 2017 renewing the approval of

difenacoum as an active substance for use in biocidal products of product-type 14. Off J Eur Union L 194:27–32
European Commission (2017c) Commission Implementing Regulation (EU) 2017/1376 of 25 July 2017 renewing the approval of warfarin as an active substance for use in biocidal products of product-type 14. Off J Eur Union L 194:9–14
European Union (2009) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. Off J Eur Union L 309:1–50
European Union (2012) Regulation (EU) No 528/2012 of the European parliament and of the council of 22 May 2012 concerning the making available on the market and use of biocidal products. Off J Eur Union L 167:1–128
Fernandez I, Santos A, Cancela ML, Laize V, Gavaia PJ (2014) Warfarin, a potential pollutant in aquatic environment acting through Pxr signaling pathway and gamma-glutamyl carboxylation of vitamin K-dependent proteins. Environ Pollut 194:86–95. https://doi.org/10.1016/j.envpol.2014.07.015
Fisher P (2013) Environmental residues of anticoagulants used for pest animal control. Landcare Research, Lincoln
Fisher P, O'Connor C, Wright GR, Eason CT (2003) Persistence of 4 anticoagulant rodenticides in the livers of laboratory rats. Department of Conservation, Wellington
Fisher P, Funnell E, Fairweather A, Brown L, Campion M (2012) Accidental discharge of brodifacoum baits into a freshwater lake: a case study. Bull Environ Contam Toxicol 88:226–228. https://doi.org/10.1007/s00128-011-0470-1
Focazio MJ, Kolpin DW, Barnes KK et al (2008) A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States-II) untreated drinking water sources. Sci Total Environ 402:201–216. https://doi.org/10.1016/j.scitotenv.2008.02.021
Fourel I, Damin-Pernik M, Benoit E, Lattard V (2017a) Core-shell LC–MS/MS method for quantification of second generation anticoagulant rodenticides diastereoisomers in rat liver in relationship with exposure of wild rats. J Chromatogr B 1041–1042:120–132. https://doi.org/10.1016/j.jchromb.2016.12.028
Fourel I, Damin-Pernik M, Benoit E, Lattard V (2017b) Cis-bromadiolone diastereoisomer is not involved in bromadiolone Red Kite (*Milvus milvus*) poisoning. Sci Total Environ 601–602:1412–1417. https://doi.org/10.1016/j.scitotenv.2017.06.011
Fournier-Chambrillon C, Berny PJ, Coiffier O et al (2004) Evidence of secondary poisoning of free-ranging riparian mustelids by anticoagulant rodenticides in France: implications for conservation of European mink (*Mustela lutreola*). J Wildl Dis 40:688–695. https://doi.org/10.7589/0090-3558-40.4.688
Fram MS, Belitz K (2011) Occurrence and concentrations of pharmaceutical compounds in groundwater used for public drinking-water supply in California. Sci Total Environ 409:3409–3417. https://doi.org/10.1016/j.scitotenv.2011.05.053
Garman GC (1991) Use of terrestrial arthropod prey by a stream-dwelling cyprinid fish. Environ Biol Fishes 30:325–331. https://doi.org/10.1007/BF02028848
Geduhn A (2015) Exposure of wildlife to anticoagulant rodenticides: how environmental drivers modulate the pathway of anticoagulant rodenticides from bait to predators. University of Münster, Münster
Geduhn A, Esther A, Schenke D, Mattes H, Jacob J (2014) Spatial and temporal exposure patterns in non-target small mammals during brodifacoum rat control. Sci Total Environ 496:328–338. https://doi.org/10.1016/j.scitotenv.2014.07.049
Geduhn A, Jacob J, Schenke D, Keller B, Kleinschmidt S, Esther A (2015) Relation between intensity of biocide practice and residues of anticoagulant rodenticides in Red Foxes (*Vulpes vulpes*). PLoS ONE 10:e0139191. https://doi.org/10.1371/journal.pone.0139191
Geduhn A, Esther A, Schenke D, Gabriel D, Jacob J (2016) Prey composition modulates exposure risk to anticoagulant rodenticides in a sentinel predator, the barn owl. Sci Total Environ 544:150–157. https://doi.org/10.1016/j.scitotenv.2015.11.117
Gibs J, Stackelberg PE, Furlong ET, Meyer M, Zaugg SD, Lippincott RL (2007) Persistence of pharmaceuticals and other organic compounds in chlorinated drinking water as a function of time. Sci Total Environ 373:240–249. https://doi.org/10.1016/j.scitotenv.2006.11.003
Godfrey E, Woessner WW, Benotti MJ (2007) Pharmaceuticals in on-site sewage effluent and ground water, Western Montana. Ground Water 45:263–271. https://doi.org/10.1111/j.1745-6584.2006.00288.x
Goldade DA, Primus TM, Johnston JJ, Zapien DC (1998) Reversed-phase ion-pair high-performance liquid chromatographic quantitation of difethialone residues in whole-body rodents with solid-phase extraction cleanup. J Agric Food Chem 46:504–508. https://doi.org/10.1021/jf970715u
Gómez-Canela C, Lacorte S (2016) Comprehensive characterization of anticoagulant rodenticides in sludge by liquid chromatography–tandem mass spectrometry. Environ Sci Pollut Res Int 23:15739–15748. https://doi.org/10.1007/s11356-016-6743-9
Gómez-Canela C, Barata C, Lacorte S (2014a) Occurrence, elimination, and risk of anticoagulant rodenticides and drugs during wastewater treatment. Environ Sci Pollut Res 21:7194–7203. https://doi.org/10.1007/s11356-014-2714-1
Gómez-Canela C, Vazquez-Chica A, Lacorte S (2014b) Comprehensive characterization of rodenticides in wastewater by liquid chromatography–tandem mass spectrometry. Anal Bioanal Chem 406:345–358. https://doi.org/10.1007/s00216-013-7449-1
Gras LM, Patergnani M, Farina M (2012) Poison-based commensal rodent control strategies in urban ecosystems: some evidence against sewer-baiting. EcoHealth 9:75–79. https://doi.org/10.1007/s10393-012-0748-8
Guan F, Ishii A, Seno H, Watanabe-Suzuki K, Kumazawa T, Suzuki O (1999) Use of an ion-pairing reagent for high-performance liquid chromatography–atmospheric pressure chemical ionization mass spectrometry determination of anionic anticoagulant rodenticides in body fluids. J Chromatogr B Biomed Sci Appl 731:155–165. https://doi.org/10.1016/S0378-4347(99)00126-7
Gurung K, Ncibi MC, Fontmorin JM (2016) Incorporating submerged MBR in conventional activated sludge process for municipal wastewater treatment: a feasibility and performance assessment. J Membr Sci Technol. https://doi.org/10.4172/2155-9589.1000158
Hauck ZZ, Feinstein DL, van Breemen RB (2016) LC-MS-MS analysis of brodifacoum isomers in rat tissue. J Anal Toxicol 40:304–309. https://doi.org/10.1093/jat/bkw008
Hernández AM, Bernal J, Bernal JL, Martín MT, Caminero C, Nozal MJ (2013) Simultaneous determination of nine anticoagulant rodenticides in soil and water by LC–ESI-MS. J Sep Sci 36:2593–2601. https://doi.org/10.1002/jssc.201300310
Horak KE, Fisher PM, Hopkins B (2018) Pharmacokinetics of anticoagulant rodenticides in target and non-target organisms. In: van den Brink NW et al (eds) Anticoagulant rodenticides and wildlife. Springer, Cham, pp 87–108
Hosea RC (2000) Exposure of non-target wildlife to anticoagulant rodenticides in California. In: Proceedings of the 19th vertebrate pest conference, pp 6–9
Huckle KR, Hutson DH, Warburton PA (1988) Elimination and accumulation of the rodenticide flocoumafen in rats following repeated oral administration. Xenobiotica 18:1465–1479. https://doi.org/10.3109/00498258809042269
Huerta B, Rodriguez-Mozaz S, Barcelo D (2012) Pharmaceuticals in biota in the aquatic environment: analytical methods and

environmental implications. Anal Bioanal Chem 404:2611–2624. https://doi.org/10.1007/s00216-012-6144-y

Hughes J, Sharp E, Taylor MJ, Melton L, Hartley G (2013) Monitoring agricultural rodenticide use and secondary exposure of raptors in Scotland. Ecotoxicol 22:974–984. https://doi.org/10.1007/s10646-013-1074-9

Hunter K (1983a) Determination of coumarin anticoagulant rodenticide residues in animal tissue by high-performance liquid chromatography: II. Fluorescence detection using ion-pair chromatography. J Chromatogr A 270:277–283. https://doi.org/10.1016/S0021-9673(01)96372-2

Hunter K (1983b) Determination of coumarin anticoagulant rodenticide residues in animal tissue by high-performance liquid chromatography: I. Fluorescence detection using post-column techniques. J Chromatogr A 270:267–276. https://doi.org/10.1016/S0021-9673(01)96372-1

Imran M, Shafi H, Wattoo SA, Chaudhary MT, Usman HF (2015) Analytical methods for determination of anticoagulant rodenticides in biological samples. Forensic Sci Int 253:94–102. https://doi.org/10.1016/j.forsciint.2015.06.008

Jacob J, Buckle A (2018) Use of anticoagulant rodenticides in different applications around the world. In: van den Brink NW et al (eds) Anticoagulant rodenticides and wildlife. Springer, Cham, pp 11–43

Jacquot M, Coeurdassier M, Couval G et al (2013) Using long-term monitoring of red fox populations to assess changes in rodent control practices. J Appl Ecol 50:1406–1414. https://doi.org/10.1111/1365-2664.12151

Jin MC, Chen XH, Zhu Y (2007) Determination of five 4-hydroxycoumarin rodenticides in animal liver tissues by ion chromatography with fluorescence detection. J Chromatogr A 1155:57–61. https://doi.org/10.1016/j.chroma.2006.12.074

Jin MC, Chen XH, Ye ML, Zhu Y (2008) Analysis of indandione anticoagulant rodenticides in animal liver by eluent generator reagent free ion chromatography coupled with electrospray mass spectrometry. J Chromatogr A 1213:77–82. https://doi.org/10.1016/j.chroma.2008.08.100

Jin MC, Cai MQ, Chen XH (2009) Simultaneous measurement of indandione-type rodenticides in human serum by liquid chromatography-electrospray ionization- tandem mass spectrometry. J Anal Toxicol 33:294–300. https://doi.org/10.1093/jat/33.6.294

Jones A (1996) HPLC determination of anticoagulant rodenticide residues in animal livers. Bull Environ Contam Toxicol 56:8–15. https://doi.org/10.1007/s001289900002

Kammerer B, Kahlich R, Ufer M, Schenkel A, Laufer S, Gleiter CH (2005) Stereospecific pharmacokinetic characterisation of phenprocoumon metabolites, and mass-spectrometric identification of two novel metabolites in human plasma and liver microsomes. Anal Bioanal Chem 383:909–917. https://doi.org/10.1007/s00216-005-0113-7

Kasprzyk-Hordern B (2010) Pharmacologically active compounds in the environment and their chirality. Chem Soc Rev 39:4466–4503. https://doi.org/10.1039/c000408c

Kinney CA, Furlong ET, Werner SL, Cahill JD (2006) Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. Environ Toxicol Chem 25:317–326. https://doi.org/10.1897/05-187R.1

Koivisto E, Koivisto P, Hanski IK et al (2016) Prevalence of anticoagulant rodenticides in non-target predators and scavengers in Finland. Finnish Safety and Chemicals Agency, Helsinki

Kolpin DW, Furlong ET, Meyer MT et al (2002) Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999–2000: a national reconnaissance. Environ Sci Technol 36:1202–1211. https://doi.org/10.1021/es011055j

Kolpin DW, Skopec M, Meyer MT, Furlong ET, Zaugg SD (2004) Urban contribution of pharmaceuticals and other organic wastewater contaminants to streams during differing flow conditions. Sci Total Environ 328:119–130. https://doi.org/10.1016/j.scitotenv.2004.01.015

Kopanke JH, Horak KE, Musselman E et al (2018) Effects of low-level brodifacoum exposure on the feline immune response. Sci Rep 8:8168. https://doi.org/10.1038/s41598-018-26558-3

Kostich MS, Lazorchak JM (2008) Risks to aquatic organisms posed by human pharmaceutical use. Sci Total Environ 389:329–339. https://doi.org/10.1016/j.scitotenv.2007.09.008

Kostich MS, Batt AL, Lazorchak JM (2014) Concentrations of prioritized pharmaceuticals in effluents from 50 large wastewater treatment plants in the US and implications for risk estimation. Environ Pollut 184:354–359. https://doi.org/10.1016/j.envpol.2013.09.013

Kotthoff M, Rüdel H, Jürling H et al (2018) First evidence of anticoagulant rodenticides in fish and suspended particulate matter: spatial and temporal distribution in German freshwater aquatic systems. Environ Sci Pollut Res Int. https://doi.org/10.1007/s11356-018-1385-8

Krüger G, Solas H (2010) Nachbarn im Kanalnetz - Ergebnisse einer Fragebogenaktion zur Rattenbekämpfung. Korrespondenz Abwasser, Abfall 57:430–435

Laasko S, Suomalainen K, Koivisto S (2010) Literature review on residues of anticoagulant rodenticides in non-target animals. Nordic Council of Ministers, Copenhagen

Lambert O, Pouliquen H, Larhantec M, Thorin C, L'Hostis M (2007) Exposure of raptors and waterbirds to anticoagulant rodenticides (difenacoum, bromadiolone, coumatetralyl, coumafen, brodifacoum): epidemiological survey in Loire Atlantique (France). Bull Environ Contam Toxicol 79:91–94. https://doi.org/10.1007/s00128-007-9134-6

Lao W, Gan J (2012) Enantioselective degradation of warfarin in soils. Chirality 24:54–59. https://doi.org/10.1002/chir.21023

Larsen J (2003) Emission scenario document for biocides used as rodenticides. Danish EPA, Copenhagen

Lemarchand C, Rosoux R, Berny P (2010) Organochlorine pesticides, PCBs, heavy metals and anticoagulant rodenticides in tissues of Eurasian otters (Lutra lutra) from upper Loire River catchment (France). Chemosphere 80:1120–1124. https://doi.org/10.1016/j.chemosphere.2010.06.026

Lemarchand C, Rosoux R, Talon C, Berny P (2014) Flagship species conservation and introduced species invasion: toxic aspects along Loire River (France). In: pesticides—toxic aspects, pp 53–79. InTech

Lewis RJ, Trager WF, Chan KK et al (1974) Warfarin stereochemical aspects of its metabolism and the interaction with phenylbutazone. J Clin Investig 53:1607–1617. https://doi.org/10.1172/jci107711

Lin Y, Shen X, Yuan Q, Yan Y (2013) Microbial biosynthesis of the anticoagulant precursor 4-hydroxycoumarin. Nat Commun 4:2603. https://doi.org/10.1038/ncomms3603

Liphatech (2013) The veterinarian's guide to accidental rodenticide ingestion by dogs & cats. Liphatech Inc., Milwaukee

Liu J, Xiong K, Ye X, Zhang J, Yang Y, Ji L (2015) Toxicity and bioaccumulation of bromadiolone to earthworm Eisenia fetida. Chemosphere 135:250–256. https://doi.org/10.1016/j.chemosphere.2015.04.058

López-Perea JJ, Camarero PR, Molina-López RA et al (2015) Interspecific and geographical differences in anticoagulant rodenticide residues of predatory wildlife from the Mediterranean region of Spain. Sci Total Environ 511:259–267. https://doi.org/10.1016/j.scitotenv.2014.12.042

Lund M (2015) Commensal rodents. In: Buckle AP, Smith RH (eds) Rodent pests and their control. CABI, Oxfordshire, pp 19–32

Magiera S, Pardylla A, Baranowska I (2015) Effects of various factors of ultrasonic treatment on the extraction recovery of drugs

from fish tissues. Ultrason Sonochem 26:388–398. https://doi.org/10.1016/j.ultsonch.2015.03.005
Mandel F, Wendt J, Vistocco R, Bachmann C (2000) Development of an LC/MS method for the analysis of rodenticides. Application note 5989-8440EN. Agilent Technologies, Waldbronn
Marek LJ, Koskinen WC (2007) Multiresidue analysis of seven anticoagulant rodenticides by high-performance liquid chromatography/electrospray/mass spectrometry. J Agric Food Chem 55:571–576. https://doi.org/10.1021/jf061440y
Market Data Forecast (2017) Europe rodenticides market by type (non-anticoagulant, anticoagulant), by mode of application (pellets, powders, sprays), by end user (agricultural fields, urban centres, warehouses, pest control companies, household consumers), and by region-Industry analysis, size, share, growth, trends, and forecasts (2016–2021). Market Data Forecast Inc., Hyderabad
Marsalek P, Modra H, Doubkova V, Vecerek V (2015) Simultaneous determination of ten anticoagulant rodenticides in tissues by column-switching UHPLC-ESI-MS/MS. Anal Bioanal Chem. https://doi.org/10.1007/s00216-015-8954-1
Maruya KA, Dodder NG, Tang C, Lao W, Tsukada D (2015) Which coastal and marine environmental contaminants are truly emerging? Environ Sci Pollut Res 22:1644–1652. https://doi.org/10.1007/s11356-014-2856-1
Masuda BM, Fisher P, Beaven B (2015) Residue profiles of brodifacoum in coastal marine species following an island rodent eradication. Ecotoxicol Environ Saf 113:1–8. https://doi.org/10.1016/j.ecoenv.2014.11.013
McDonald RA, Harris S, Turnbull G, Brown P, Fletcher M (1998) Anticoagulant rodenticides in stoats (*Mustela erminea*) and weasels (*Mustela nivalis*) in England. Environ Pollut 103:17–23. https://doi.org/10.1016/S0269-7491(98)00141-9
McLeod L, Saunders G (2013) Pesticides used in the management of vertebrate pests in australia: a review. NSW Department of Primary Industries, New South Wales
Medvedovici A, David F, Sandra P (1997) Determination of the rodenticides warfarin, diphenadione and chlorophacinone in soil samples by HPLC-DAD. Talanta 44:1633–1640. https://doi.org/10.1016/S0039-9140(97)00068-4
Morrison SA, Sieve KK, Ratajczak RE, Bringolf RB, Belden JB (2016) Simultaneous extraction and cleanup of high-lipid organs from white sturgeon (Acipenser transmontanus) for multiple legacy and emerging organic contaminants using QuEChERS sample preparation. Talanta 146:16–22. https://doi.org/10.1016/j.talanta.2015.08.021
Murphy G, Oldbury DJ (2002) Rat control by local authorities within the United Kingdom. In: Proceedings of the 4th international conference on urban pests,vol 246, pp 413–420
Murray M (2011) Anticoagulant rodenticide exposure and toxicosis in four species of birds of prey presented to a wildlife clinic in Massachusetts, 2006–2010. J Zoo Wildl Med 42:88–97
Nakagawa L, de Masi E, Narciso E, Neto HM, Papini S (2015) Palatability and efficacy of bromadiolone rodenticide block bait previously exposed to environmental conditions. Pest Manag Sci 71:1414–1418. https://doi.org/10.1002/ps.3944
Newton I, Wyllie I, Freestone P (1990) Rodenticides in British barn owls. Environ Pollut 68:101–117. https://doi.org/10.1016/0269-7491(90)90015-5
Newton I, Wyllie I, Dale L (1997) Mortality causes in British Barn Owls (Tyto alba), based on 1,101 carcasses examined during 1963–1996. United States Department of Agriculture Forest Service, Winnipeg, pp 299–307
Norström K, Remberger M, Kaj L et al (2009) Results from the Swedish National Screening Programme 2008. Subreport 3. Biocides: difenacoum. IVL Swedish Environmental Research Institute, Stockholm
Ogilvie SC, Pierce RJ, Wright GRG, Booth LH, Eason CT (1997) Brodifacoum residue analysis in water, soil, invertebrates, and birds after rat eradication on Lady Alice Island. N Z J Ecol 21:195–197
Oktay E (2015) Will NOACs become the new standard of care in anticoagulation therapy? Int J Cardiovasc Acad 1:1–4. https://doi.org/10.1016/j.ijcac.2015.06.007
Ondracek K, Bandouchova H, Hilscherova K et al (2015) Mixture toxicity of microcystin-LR, paraoxon and bromadiolone in *Xenopus laevis* embryos. Neuro Endocrinol Lett 36:114–119
Parker R (2013) Gute Aussichten für die Zukunft. DpS 2:13–15
Pérez S, Barceló D (2008) Applications of LC-MS to quantitation and evaluation of the environmental fate of chiral drugs and their metabolites. TrAC Trends Anal Chem 27:836–846. https://doi.org/10.1016/j.trac.2008.09.003
Pieper C, Holthenrich D, Schneider H (2014) Health risks from pest control products. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 57:574–584. https://doi.org/10.1007/s00103-013-1920-1
Pitt WC, Berentsen AR, Shiels AB et al (2015) Non-target species mortality and the measurement of brodifacoum rodenticide residues after a rat (*Rattus rattus*) eradication on Palmyra Atoll, tropical Pacific. Biol Conserv 185:36–46. https://doi.org/10.1016/j.biocon.2015.01.008
Primus TM, Wright G, Fisher P (2005) Accidental discharge of brodifacoum baits in a tidal marine environment: a case study. Bull Environ Contam Toxicol 74:913–919. https://doi.org/10.1007/s00128-005-0668-1
Ramirez AJ, Brain RA, Usenko S et al (2009) Occurrence of pharmaceuticals and personal care products in fish: results of a national pilot study in the United States. Environ Toxicol Chem 28:2587–2597. https://doi.org/10.1897/08-561.1
Rattner BA, Mastrota FN (2018) Anticoagulant rodenticide toxicity to non-target wildlife under controlled exposure conditions. In: van den Brink NW et al (eds) Anticoagulant rodenticides and wildlife. Springer, Cham, pp 45–86
Rattner BA, Lazarus RS, Elliott JE, Shore RF, van den Brink N (2014) Adverse outcome pathway and risks of anticoagulant rodenticides to predatory wildlife. Environ Sci Technol 48:8433–8445. https://doi.org/10.1021/es501740n
Sage M, Fourel I, Coeurdassier M, Barrat J, Berny P, Giraudoux P (2010) Determination of bromadiolone residues in fox faeces by LC/ESI-MS in relationship with toxicological data and clinical signs after repeated exposure. Environ Res 110:664–674. https://doi.org/10.1016/j.envres.2010.07.009
Sanchez-Barbudo IS, Camarero PR, Mateo R (2012) Primary and secondary poisoning by anticoagulant rodenticides of non-target animals in Spain. Sci Total Environ 420:280–288. https://doi.org/10.1016/j.scitotenv.2012.01.028
Santos LH, Gros M, Rodriguez-Mozaz S et al (2013) Contribution of hospital effluents to the load of pharmaceuticals in urban wastewaters: identification of ecologically relevant pharmaceuticals. Sci Total Environ 461:302–316. https://doi.org/10.1016/j.scitotenv.2013.04.077
Sato S (2005) Coumarin rodenticides. In: Suzuki O, Watanabe K (eds) Drugs and poisons in humans. Springer, Heidelberg, pp 599–608
Schaff JE, Montgomery MA (2013) An HPLC-HR-MS-MS method for identification of anticoagulant rodenticides in blood. J Anal Toxicol 37:321–325. https://doi.org/10.1093/jat/bkt036
Schmolz E, Wieck S, Friesen A (2014) Nagetierbekämpfung mit Antikoagulanzien—was ändert sich durch die Biozid-Zulassung für die Praxis? UMID 2:79–86
Schwabe U, Paffrath D, Ludwig W-D, Klauber J (eds) (2017) Arzneiverordnungs-report. Springer, Heidelberg
Shore RF, Birks JDS, Afsar A, Wienburg CL, Kitchener AC (2003) Spatial and temporal analysis of second-generation anticoagulant

rodenticide residues in polecats (Mustela putorius) from throughout their range in Britain, 1992–1999. Environ Pollut 122:183–193. https://doi.org/10.1016/S0269-7491(02)00297-X

Siers SR, Shiels AB, Goldade DA et al (2016) Wake atoll fish tissue sampling and analysis three years after an island wide rodenticide application. Unpublished Report QA 2241, USDA, APHIS, WS, National Wildlife Research Center, Hilo, HI, USA

Smith LL, Liang B, Booth MC, Filigenzi MS, Tkachenko A, Gaskill CL (2017) Development and validation of quantitative ultraperformance liquid chromatography-tandem mass spectrometry assay for anticoagulant rodenticides in liver. J Agric Food Chem 65:6682–6691. https://doi.org/10.1021/acs.jafc.7b02280

Steffen D (2014) Orientierende Untersuchungen niedersächsischer Oberflächengewässer auf aktuell in Deutschland zugelassener Pflanzenschutzmittel und auf Stoffe der sog. Metaboliten-Liste. Niedersächsischer Landesbetrieb für Wasserwirtschaft, Küsten- und Naturschutz (NLWKN), Hannover-Hildesheim, Germany

Streit B (1998) Bioaccumulation of contaminants in fish. In: Braunbeck T, Hinton DE, Striet B (eds) Fish ecotoxicology. Birkhäuser, Basel

Tosh DG, McDonald RA, Bearhop S et al (2011) Does small mammal prey guild affect the exposure of predators to anticoagulant rodenticides? Environ Pollut 159:3106–3112. https://doi.org/10.1016/j.envpol.2011.03.028

Tosh DG, McDonald RA, Bearhop S, Llewellyn NR, Montgomery WI, Shore RF (2012) Rodenticide exposure in wood mouse and house mouse populations on farms and potential secondary risk to predators. Ecotoxicology 21:1325–1332. https://doi.org/10.1007/s10646-012-0886-3

Townsend MG, Entwisle P, Hart ADM (1995) Use of two halogenated biphenyls as indicators of non-target exposure during rodenticides treatments. Bull Environ Contam Toxicol 54:526–533. https://doi.org/10.1007/BF00192595

UBA (2011) Identifizierung und Bewertung ausgewählter Arzneimittel und ihrer Metaboliten (Ab- und Umbauprodukte) im Wasserkreislauf. Texte 46/2011, Umweltbundesamt, Dessau-Roßlau

UBA (2014) Authorisation of anticoagulant rodenticides in Germany—risk mitigation measures, best practice code and FAQs. Umweltbundesamt, Dessau-Roßlau

van den Brink NW, Elliott JE, Shore RF, Rattner BA (eds) (2018) Anticoagulant rodenticides and wildlife. Springer, Cham

Vudathala D, Cummings M, Murphy L (2010) Analysis of multiple anticoagulant rodenticides in animal blood and liver tissue using principles of QuEChERS Method. J Anal Toxicol 34:273–279. https://doi.org/10.1093/jat/34.5.273

Walker LA, Turk A, Long SM, Wienburg CL, Best J, Shore RF (2008) Second generation anticoagulant rodenticides in tawny owls (*Strix aluco*) from Great Britain. Sci Total Environ 392:93–98. https://doi.org/10.1016/j.scitotenv.2007.10.061

Walker LA, Llewellyn NR, Pereira MG et al (2010) Anticoagulant rodenticides in predatory birds 2007 and 2008: a Predatory Bird Monitoring Scheme (PBMS) report. Center for Ecology and Hydrology, Lancaster

Wardlaw J, Hughes J, Monie C, Reay G (2016) Pesticide usage in Scotland—rodenticide use by local authorities 2015. Science and Advice for Scottish Agriculture, Edinburgh

Wardlaw J, Hughes J, Monie C, Reay G (2017) Pesticide usage in Scotland—rodenticides on arable farms 2016. Science and Advice for Scottish Agriculture, Edinburgh

Watkins CD, Winemiller KO, Mora MA et al (2014) Assessment of mosquitofish (Gambusia affinis) health indicators in relation to domestic wastewater discharges in suburbs of Houston, USA. Bull Environ Contam Toxicol 93:13–18. https://doi.org/10.1007/s00128-014-1248-z

Weigt S, Huebler N, Strecker R, Braunbeck T, Broschard TH (2012) Developmental effects of coumarin and the anticoagulant coumarin derivative warfarin on zebrafish (Danio rerio) embryos. Reprod Toxicol 33:133–141. https://doi.org/10.1016/j.reprotox.2011.07.001

Wode F, van Baar P, Dunnbier U et al (2015) Search for over 2000 current and legacy micropollutants on a wastewater infiltration site with a UPLC-high resolution MS target screening method. Water Res 69:274–283. https://doi.org/10.1016/j.watres.2014.11.034

Wong LT, Solomonraj G (1980) Biliary and urinary excretion of [14C]warfarin in rabbits. Xenobiotica 10:201–210. https://doi.org/10.3109/00498258009033746

Zielinska A, Lichti CF, Bratton S et al (2008) Glucuronidation of monohydroxylated warfarin metabolites by human liver microsomes and human recombinant UDP glucuronosyltransferases. J Pharmacol Exp Ther 324:139–148. https://doi.org/10.1124/jpet.107.129858

From:	Thomas Tomeoni
To:	Coastal Strategic Plan Comments
Subject:	Redraw the limits of the Coastal Zone
Date:	Friday, October 30, 2020 7:29:15 PM

No where in the draft Strategic Plan is there any consideration for redrawing the boundary of the Coastal Zone.

After 50 years of operation the biggest issue that limits the efficient and effective operation of the Coastal Zone is the consistent lack of resources for staff and studies for implementing almost 200 line items of proposed goals and objectives.

If the area of the Coastal Zone were dramatically decreased in urban areas local jurisdictions and property owners would be unburdened of CCC often arbitrary and otherwise irrelevant restrictions on every project large and small.

In turn the CCC staff would be relieved of trivial projects with little or no benefit to the more important strategic goals of preserving the most environmentally valuable coastal resources.

If the numbers of permits required was reduced by 50 % the corresponding savings in staff and commissioners time could be redirected to the most relevant work with the greatest benefit to all communities in the Coastal region.

Consider reducing the area of the Coastal Zone with the least impact on Coastal Zone resources.

Tom Tomeoni
Thousand Oaks

From:	Dwight Worden
To:	Coastal Strategic Plan Comments
Subject:	CCC AStrategic Plan: Comments
Date:	Monday, November 2, 2020 9:17:16 AM

Dear CCC:
I reviewed your final draft Strategic Plan. Overall, I find it very well done. One suggestion: I see no mention of coastal railroad issues. I suggest the Commission consider adding language in the appropriate place in support of its traditional role of applying federal consistency review to coastal railroad projects, and of requiring CDPs either at the local government level where a certified LCP so requires, or at the Commission level where a CDP and not just federal consistency review is required (for example, on projects outside the rail right-of-way). I think the Commission and public would be well served if the Commission were to be clear on these issues in light of the recent challenges to the Commission's authority in this area.

Thanks!
Dwight Worden

From:	Jayne Lane
To:	Coastal Strategic Plan Comments; Padilla, Stephen@Coastal
Cc:	Lou Galuppo; Kristin Miller; Elysian Kurnik; Terah Drent
Subject:	Comments On the Commission"s 2021-2025 Proposed Final Strategic Plan
Date:	Wednesday, November 4, 2020 12:38:53 PM
Attachments:	image002.png image003.png 2020-11-03 Ltr re CCC Final Strategic Plan G10GL.pdf

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Good Afternoon:

Please see attached letter from Beach Cities Preservation Alliance.

Sincerely,

Jayne Lane
Legal Secretary/Paralegal
G10 GALUPPO LAW
Lawyers, Counselors, and Advisors
a Professional Law Corporation
2792 Gateway Road
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Beach Cities
Preservation Alliance

Tuesday, November 3, 2020

Via Email: StrategicPlanComments@coastal.ca.gov
Stephen.Padilla@coastal.ca.gov

Mr. Steve Padilla, Chairman
California Coastal Commission
1121 "L" Street, Suite 503
Sacramento, CA 95814

SUBJECT: Comments on the Commission's 2021-2025 Proposed Final Strategic Plan

Dear Mr. Padilla and Commission Staff:

Our organization has reviewed the 2021-2025 Proposed Final Strategic Plan and are extremely concerned that **the plan is silent as to the rights of existing coastal property owners**. Pursuant to Section 30235 of the Coastal Act, "revetments, breakwaters, groins, harbor channels, seawalls, cliff retaining walls, and other such construction that alters natural shoreline processes shall be permitted when required to serve coastal-dependent uses or to **protect existing structures** or public beaches in danger from erosion…" (emphasis added). Therefore, our preliminary comments are as follows:

- **Goals, pg. 3**. Add a tenth goal (Goal 10), Protect the Constitutional Rights of Existing Landowners, to address the constitutional rights of property owners to protect their property from rising sea levels and related flooding.
- **Objective 4.6**. We agree with the objective to increase public awareness and participation to address climate change, but the education must include the potential effects of climate change on existing development and the constitutional rights of private property owners to protect their properties.
- **Objective 6.3**. Add a policy under this objective to address the protection of existing development.

Again, individuals have an inalienable constitutional right to protect their properties. The Strategic Plan needs to address this fact more often and with more specificity, especially given the potential of sea level rise to impact properties along the California coastline.

Thank you for your consideration of our comments.

Sincerely,

LOUIS A. GALUPPO
Director of Education, Legal, and Governmental Affairs

2792 GATEWAY ROAD, SUITE 106 • CARLSBAD, CALIFORNIA 92009 • P. 760 431 4575 • F. 760 431 4579

From:	Cordova, Lorenzo
To:	Coastal Strategic Plan Comments; Rice, Katie@Coastal; Manna, Jeannine@Coastal
Cc:	Rodoni, Dennis; Lai, Thomas; Jennifer Blackman
Subject:	Letter of Support for ACMV
Date:	Wednesday, November 4, 2020 3:54:06 PM
Attachments:	ACMV Letter re CCC Strategic Plan 2021-2015.pdf ccc_strategicplan_11042020final.pdf

Hello Commissioner Rice, Coastal Commissioners, and Jeannine:

Supervisor Rodoni would like to respectfully submit this letter of support on behalf of the Alliance of Coastal Marin Villages re: their comments to the CCC Final Strategic Plan 2021-2025. Thank you for your consideration.

Best,
Lorenzo

LORENZO G. CORDOVA| He/Him/His
Office of Supervisor Dennis Rodoni, 4th Dist.
T: (415) 473-3092
E: lcordova@marincounty.org
3501 Civic Center Drive, Suite 326
San Rafael CA, 94903
COUNTY OF MARIN

COUNTY OF MARIN

BOARD OF SUPERVISORS

November 4, 2020

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Katie Rice, Commissioner
California Coastal Commission
45 Fremont Street
San Francisco, CA 94105
Sent via email

Subject: Letter of Support for the Alliance of Coastal Marin Villages (ACMV)'s Comments on the Coastal Commission Final Strategic Plan 2021-2025

Dear Commissioner Rice:

I write in support of the recent letter submitted on November 4th, 2020 by the Alliance of Coastal Marin Villages (ACMV)'s regarding the Coastal Commission Final Strategic Plan 2021-2025. A copy of this letter has been attached. The ACMV is representative of our coastal villages in Marin and they have dedicated their time to thoroughly analyze the strategic plan.

In addition, the County of Marin is fully committed to equity in all its planning and actions. We strongly support Goal 5 for advancing diversity, equity, environmental justice, and tribal relations. We suggest you add one other objective in this regard - seeking to develop a better understanding of how underserved communities use our beaches and coastlines, identifying any impediments to that use, and developing ways to expand their opportunities.

I respectfully ask that you take into consideration these comments.

Sincerely,

Dennis Rodoni, District 4
Marin County Board of Supervisors

Thomas Lai, Interim Director
Marin County Community Development Agency

From:	Jennifer Blackman
To:	krice@marincounty.org
Cc:	Padilla, Stephen@Coastal; Brownsey, Donne@Coastal; Aminzadeh, Sara@Coastal; Dayna.Bochco@coastal.ca.gove; Escalante, Linda@Coastal; Groom, Carole@Coastal; Hart, Caryl@Coastal; Howell, Erik@Coastal; Rice, Katie@Coastal; Effie.Turnball-Sanders@coastal.ca.gov; Uranga, Roberto@Coastal; Wilson, Mike@Coastal; Rodoni, Dennis; Coastal Strategic Plan Comments
Subject:	Letter from the Alliance of Coastal Marin Villages - CCC Proposed Final 2021-25 Strategic Plan
Date:	Wednesday, November 4, 2020 3:56:51 PM
Attachments:	ACMV Letter re CCC Strategic Plan 2021-2015.pdf Letters from ACMV, Rodoni and Crawford re Strategic Plan2.pdf

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Dear Commissioner Rice:

Attached please find a letter from the Alliance of Coastal Marin Villages on the California Coastal Commission's Proposed Final 2021-2025 Strategic Plan, Item 5 on the November 6, 2020 Commission meeting agenda.

Best regards,

Jennifer Blackman
Chair, Alliance of Coastal Marin Villages

Alliance of Coastal Marin Villages

Bolinas, Dillon Beach, Inverness, Inverness Park, Marshall, Muir Beach, Olema, Point Reyes Station, Stinson Beach, Tomales

November 4, 2020

Via email: krice@marincounty.org and Katie.Rice@coastal.ca.gov

Commissioner Katie Rice
California Coastal Commission
Executive Division
455 Market Street
Suite 300
San Francisco, California 94105

Re: California Coastal Commission Final Strategic Plan 2021-2025.

Dear Commissioner Rice:

Thank you very much for virtually meeting with representatives of the Alliance of Coastal Marin Villages ("ACMV") on November 3, 2020 and for listening to our concerns about key omissions in the California Coastal Commission ("CCC") Final Strategic Plan 2021-2025 ("Strategic Plan"). As you requested, we write this letter to provide you with a brief summary of our concerns, which previously were expressed in correspondence submitted to the CCC in February 2020 by the ACMV, several village associations, Marin County Supervisor Dennis Rodoni and the Marin County Community Development Agency with regard to the Public Review Draft of the Strategic Plan (version 12/6/19). Copies of that prior correspondence are attached to this letter for your ease of reference.

First and foremost, we believe the Strategic Plan is flawed as a consequence of its failure to prioritize the preservation of a critical coastal resource: the unique coastal communities that serve to attract millions of coastal visitors. (Note: coastal communities are referred to in the Coastal Act in some places as "special" and/or the "character" of the communities is referenced in other documents – this language is outdated and carries with it connotations of privilege the ACMV does not endorse. To the extent we used this language in prior letters, it has only been to quote directly from the Coastal Act or other related documents). The omission of coastal communities as a coastal resource warranting protection appears to have been a deliberate decision by CCC staff because the 2013-2018 Strategic Plan (approved by the Commission in April 2013), states:

> "The Commission will continue to protect **all of the resources identified for such in the Coastal Act,** including scenic resources and **community character**, cultural resources, and protection of coastal-dependent land uses to name a few. The Commission's vision for the coast embodies all of the goals and policies of the Coastal Act, and it will continue to do its utmost to apply the entirety of the Act as necessary in any regulatory or planning matter before it. The Commission is deeply committed to sustaining and building on its forty-year history of successful coastal protection and management in California."

Coastal staff's memo dated October 22, 2020 concerning the changes made to the Strategic Plan notes on page 5 that: "new language was added to Action 2.2.4 to specify that work with partner agencies will include addressing impacts of high visitation along roadways and in coastal communities." This is unsatisfactory as the referenced language is in the Goal 2, Public Access section of the Strategic Plan, not Goal 3, Coastal Resources. Moreover, the actual language seems to narrowly construe the "solution" for addressing the impacts of increased visitation on coastal communities solely as providing access-related facilities in those communities.

We submit that *mitigating the impacts of increased visitation should include protection of coastal communities -- as coastal resources – from the challenging effects of that increased visitation (i.e., traffic congestion, excessive garbage, impacts on water and wastewater systems, and so forth).* **We therefore urge the Commission to reinstate the protection of unique coastal communities as a priority in both the Strategic Plan Vision Statement and Goal 3, as outlined in our February 6, 2020 comment letter, reflecting the mandate of Section 30253(e) of the Coastal Act to " . . . protect special communities and neighborhoods that, because of their unique characteristics, are popular visitor destination points for recreational uses."** Specifically, we ask that an additional Objective be added to the Strategic Plan, "Coastal Resources – Goal 3 -- Protect and Enhance Coastal Resources":

Objective 3.x Protect the Unique Character of Special Communities and Neighborhoods.

3.x.1 Update LCP guidance on protection of special communities and neighborhoods that, because of their unique characteristics, are popular visitor destination points for recreational uses.

3.x.2 Encourage sensible management solutions and sources of financial support where increased coastal tourism threatens environmental resources, the character of coastal communities, the financial ability of local agencies to serve tourist needs, and/or the visitor experience.

3.x.3 Outreach to coastal communities to promote information-sharing on key issues relating to the management of increasing tourism through guidance documents, webinars, and/or workshops.

Like the protections of Objective 3.3 for agriculture (which served as a model for this proposed objective), including this Objective in the Strategic Plan would ensure that the CCC and its staff will not fail to implement the important protections for coastal communities granted under the Coastal Act.

These coastal resources protections are of such importance to our communities and others along the California coast that they should also be mentioned in the Vision Statement on page 8. In our February 2020 comment letter on the Public Review Draft, we proposed this addition:

Our Vision:

The California coast is available for all to enjoy through thousands of public accessways to and along the shoreline, a completed California Coastal Trail, a well-supported network of parks and open spaces, and a wide range of visitor-serving facilities, including lower-cost campgrounds, hostels, and hotels. The rich ecological diversity of the coast and ocean, including beaches, rocky shorelines, wetlands, riparian areas, and sensitive terrestrial habitats, is protected and thriving. Scenic rural landscapes are maintained, coastal agriculture is flourishing, **the unique characteristics of the special communities and neighborhoods that attract coastal visitors are preserved**, and cultural resources are protected. The California Coastal Commission works collaboratively with local governments, other agencies, and an engaged and knowledgeable public committed to coastal stewardship to support and manage environmentally-sustainable development, including assuring priority for coastal-dependent and related uses of land and water, concentrating new growth in existing urban areas, providing multi-modal public access and transportation, and promoting well-adapted, resilient communities in the face of global climate change. The coast endures as a vital part of California's social and cultural fabric and the coastal and ocean economy is strong.

We reiterate that proposal and further recommend that sixth sentence of the paragraph below the Vision Statement on page 8, be revised to read as follows: "New development should be concentrated in existing developed areas (30250) **and be consistent with the unique characteristics of coastal communities (30253(e))**;".

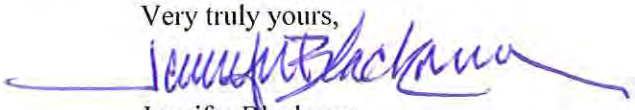
Second, the ACMV believes that another flaw in the Strategic Plan is its failure to explicitly acknowledge the California Legislature's findings in Section 30604(g) of the Coastal Act, specifically:

> *"The Legislature finds and declares that it is important for the commission to encourage the protection of existing and the provision of new affordable housing opportunities for persons of low and moderate income in the coastal zone."*

The ACMV endorses the comments of the Bolinas Community Public Utility District (a member of the ACMV) in its comment letter dated February 10, 2020 on the Public Review Draft, which noted that the preservation and promotion of affordable housing is almost entirely unmentioned in the Strategic Plan: "***The Commission should correct this oversight and include a set of objectives to work with local communities to protect and expand the development of affordable housing in the coastal zone because we believe that the coastal zone should not be the domain of only the most wealthy Californians***." Indeed, as the BCPUD noted in its letter, such a result would be inconsistent with the Environmental Justice mandate of the Coastal Act addressed in Goal 5 of the Draft Plan. Although a few references to "housing affordability" have been added to Goal 6 in the Strategic Plan, we believe this language does not sufficiently prioritize the urgent need to rebalance the availability of housing in the coastal zone in favor of lower income residents, who are often among the most vulnerable and disadvantaged in our communities. To that end, the ACMV submits that **locally available and affordable housing for agricultural workers in the coastal zone also should be expressly addressed and prioritized in Goal 3, Objective 3.3, consistent with Environmental Justice principles and the Commission's prioritization of the protection of coastal agriculture**.

Finally, we respectfully submit that the new language added to the Strategic Plan regarding Covid-19 contains a significant inaccuracy insofar as it asserts that the pandemic "has reduced the demand for visitor-serving uses such as hotels, short-term rentals, and public transportation, and resulted in the direct closure or strict limitations of other visitor-serving uses such as visitor centers, museums and temporary events." While there may have been a fleeting reduction of demand for visitor-serving uses at the outset of the pandemic, those of us who live in the coastal communities see no continuing evidence of this at this time.

Very truly yours,



Jennifer Blackman
Chair, Alliance of Coastal Marin Villages

cc: Supervisor Dennis Rodoni, Marin County Board of Supervisors, District 4, drodoni@marincounty.org
Steve Padilla, Chair, California Coastal Commission, Stephen.Padilla@coastal.ca.gov
Donne Brownsey, Vice Chair, California Coastal Commission, Donne.Brownsey@coastal.ca.gov
Sara Aminzadeh, Commissioner, California Coastal Commission, Sara.Aminzadeh@coastal.ca.gov
Dayna Bochco, Commissioner, California Coastal Commission, Dayna.Bochco@coastal.ca.gov
Linda Escalante, Commissioner, California Coastal Commission, Linda.Escalante@coastal.ca.gov
Carole Groom, Commissioner, California Coastal Commission, Carole.Groom@coastal.ca.gov
Dr. Caryl Hart, Commissioner, California Coastal Commission, Caryl.Hart@coastal.ca.gov
Erik Howell, Commissioner, California Coastal Commission, Erik.Howell@coastal.ca.gov
Effie Turnball-Sanders, Commissioner, California Coastal Commission, Effie.Turnball-Sanders@coastal.ca.gov
Roberto Uranga, Commissioner, California Coastal Commission, Roberto.Uranga@coastal.ca.gov
Mike Wilson, Commissioner, California Coastal Commission, Mike.Wilson@coastal.ca.gov
StrategicPlanComments@coastal.ca.gov

Alliance of Coastal Marin Villages

Bolinas, Dillon Beach, Inverness, Inverness Park, Marshall, Muir Beach, Olema, Point Reyes Station, Stinson Beach, Tomales

February 6, 2020

California Coastal Commission
Executive Division
45 Fremont Street, Suite 2000
San Francisco, CA 94105

By email to: StrategicPlanComments@coastal.ca.gov

Re: Comments on the Public Review Draft California Coastal Commission Strategic Plan 2020-2025.

Dear California Coastal Commission, Executive Division:

The Alliance of Coastal Marin Villages ("ACMV") consists of representatives of all the villages located in unincorporated West Marin County that are in the Coastal Zone: Bolinas, Dillon Beach, Inverness, Inverness Park, Marshall, Muir Beach, Olema, Point Reyes Station, Stinson Beach and Tomales. The ACMV formed as a result of meetings convened by California State Senator Mike McGuire to assess the impacts of (and formulate solutions to) the problems posed by increased tourism to West Marin, which has strained local resources and degraded the coastal visitation experience. The ACMV meets regularly to discuss and address issues of common concern, and on a quarterly basis with Marin County Supervisor Dennis Rodoni.

We write today to urge the California Coastal Commission ("CCC") and its staff to correct an omission in the draft Strategic Plan for 2020 – 2025 (version 12/6/19). The Strategic Plan should include a Goal and several Objectives in accordance with the statutory direction of PRC §30253(e):

> *§30253 New development shall do all of the following:*
>
> ... .
>
> *(e) Where appropriate, protect special communities and neighborhoods that, because of their unique characteristics, are popular visitor destination points for recreational uses.*

As stated in Marin County's Local Coastal Plan with respect to PRC§ 30253: "[t]he intent of this policy is to protect the unique character of existing coastal communities." Almost all of our villages are special communities that, because of their unique characteristics, are popular visitor destinations. Like similar small villages up and down the California coast, these villages are suffering the consequences of substantially increased numbers of coastal visitors — numbers far greater than when the Coastal Act became law.[1] The villages need protection and relief from the effects of increasing numbers of recreational visitors. The villages face significant financial and logistical challenges to providing services to the additional visitors while at the same time protecting the coastal environment and maintaining their community character. Indeed, it is the very special character of these villages that makes them such popular visitor destinations in the first place.

Increasing tourism to our communities has these impacts: excessive trash; stress on local water and sanitation systems; the need for more public bathrooms; traffic congestion; traffic-related threats to public safety; noise and disturbance of fragile local ecosystems; and parking challenges for visitors and locals alike. Addressing

[1] The impacts of increased tourism to our area caused the Marin County Board of Supervisors to underwrite a study, AECOM, "West Marin Visitor Needs Assessment" (May 2017), which predicted substantial growth in visitor numbers in the years ahead. Senator Mike McGuire hosted overflow meetings on the subject in Point Reyes Station in 2017 and 2019.

these impacts often exceeds the capacity of existing infrastructure and local financial resources. As directed by the Coastal Act, the CCC needs to balance the laudable goal of preserving public access against these impacts to ensure there is reasonable management of public access, financial resources for impacted communities to retain their special character, and attention to these consequences in connection with new development and other CCC policies.

Thus, in accordance with Coastal Act Section 30253(e), we ask that an additional Objective be added to the Draft Strategic Plan, "Coastal Resources – Goal 3 -- Protect and Enhance Coastal Resources":

Objective 3.x Protect the Unique Character of Special Communities and Neighborhoods.

3.x.1 Update LCP guidance on protection of special communities and neighborhoods that, because of their unique characteristics, are popular visitor destination points for recreational uses.

3.x.2 Encourage sensible management solutions and sources of financial support where increased coastal tourism threatens environmental resources, the character of coastal communities, the financial ability of local agencies to serve tourist needs, and/or the visitor experience.

3.x.3 Outreach to coastal communities to promote information-sharing on key issues relating to the management of increasing tourism through guidance documents, webinars, and/or workshops.

Like the protections of Objective 3.3 for agriculture (which served as a model for this proposed objective), including this Objective in the Strategic Plan 2020-2025 would ensure that the CCC and its staff will not fail to address the important protections for coastal communities granted under the Coastal Act.

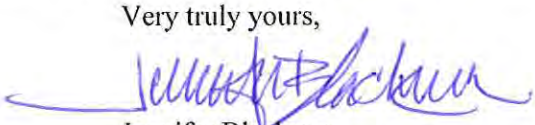
These protections are of such importance to our villages and others along the California coast that they should also be mentioned in the Vision Statement. We propose this addition:

Our Vision:

The California coast is available for all to enjoy through thousands of public accessways to and along the shoreline, a completed California Coastal Trail, a well-supported network of parks and open spaces, and a wide range of visitor-serving facilities, including lower-cost campgrounds, hostels, and hotels. The rich ecological diversity of the coast and ocean, including beaches, rocky shorelines, wetlands, riparian areas, and sensitive terrestrial habitats, is protected and thriving. Scenic rural landscapes are maintained, coastal agriculture is flourishing, the unique characteristics of the special communities and neighborhoods that attract coastal visitors are preserved, and cultural resources are protected. The California Coastal Commission works collaboratively with local governments, other agencies, and an engaged and knowledgeable public committed to coastal stewardship to support and manage environmentally-sustainable development, including assuring priority for coastal-dependent and related uses of land and water, concentrating new growth in existing urban areas, providing multi-modal public access and transportation, and promoting well-adapted, resilient communities in the face of global climate change. The coast endures as a vital part of California's social and cultural fabric and the coastal and ocean economy is strong.

In closing, the members of the ACMV believe that the failure of the Draft Strategic Plan to specifically include an objective to preserve the special character of coastal communities and neighborhoods is an omission that needs to be corrected, and we respectfully request that the Commission and CCC staff revise the Draft Strategic Plan accordingly. Please contact me with any questions or if you would like more information about the ACMV. Thank you very much for this opportunity to comment on the Draft Strategic Plan.

Very truly yours,



Jennifer Blackman
Chair, Alliance of Coastal Marin Villages

cc: Supervisor Dennis Rodoni, Marin County Board of Supervisors, District 4, drodoni@marincounty.org
Senator Mike McGuire, California State Senate, District 2, senator.mcguire@senate.ca.gov
Assemblymember Marc Levine, California State Assembly, District 10, assemblymember.levine@assembly.ca.gov
Steve Padilla, Chair, California Coastal Commission, Stephen.Padilla@coastal.ca.gov
Donne Brownsey, Vice Chair, California Coastal Commission, Donne.Brownsey@coastal.ca.gov
Sara Aminzadeh, Commissioner, California Coastal Commission, Sara.Aminzadeh@coastal.ca.gov
Dayna Bochco, Commissioner, California Coastal Commission, Dayna.Bochco@coastal.ca.gov
Linda Escalante, Commissioner, California Coastal Commission, Linda.Escalante@coastal.ca.gov
Carole Groom, Commissioner, California Coastal Commission, Carole.Groom@coastal.ca.gov
Dr. Caryl Hart, Commissioner, California Coastal Commission, Caryl.Hart@coastal.ca.gov
Erik Howell, Commissioner, California Coastal Commission, Erik.Howell@coastal.ca.gov
Katie Rice, Commissioner, California Coastal Commission, Katie.Rice@coastal.ca.gov
Effie Turnball-Sanders, Commissioner, California Coastal Commission, Effie.Turnball-Sanders@coastal.ca.gov
Roberto Uranga, Commissioner, California Coastal Commission, Roberto.Uranga@coastal.ca.gov
Mike Wilson, Commissioner, California Coastal Commission, Mike.Wilson@coastal.ca.gov

COUNTY OF MARIN

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February 11, 2020

California Coastal Commission, Executive Division
45 Fremont Street, Suite 2000
San Francisco, CA 94105

By email: StrategicPlanComments@coastal.ca.gov
Re: California Coastal Commission Strategic Plan 2020-2025
Public Draft Comments

Dear California Coastal Commission Executive Division:

As District 4 Supervisor and representative for Marin County's coast, I respectfully submit these comments for the public draft of your Strategic Draft 2020-2025. My desire to make these comments are both personal and professional. I am fourth generation West Marin resident and Olema has been my home for 27 years. I have dedicated my career to protecting our coast; often partnering with key stakeholders and village community leaders to develop solutions on the most pressing issues facing our California coast.

It is difficult to measure the impact of our dedicated local village groups. However, our coastal village groups have been leaders in coastal protection and management, even prior to the 1976 California Coastal Act. Like our ranching community's direct involvement in the transformation of the Marin Peninsula into the Pt. Reyes National Seashore, our local village groups were instrumental in the successful passing of 1976 California Coastal Act. Their unique perspective as actual coastal village residents should not be underestimated nor ignored by this plan. Instead, this plan should reflect their direct commitment to developing formidable solutions to issues affecting our Marin County coast.

Thus, my office is supportive of the comments proposed by local village groups, like those suggested by the Alliance of Marin Coastal Villages (ACMV), Bolinas Public Utilities District (BCPUD), Muir Beach Community Services District (MBCSD), and East Shore Planning Group (ESPG). Please allow me the opportunity to reiterate some their partial comments and include some of my suggested feedback to your plan.

Alliance of Marin Coastal Villages

Increasing tourism to our communities has these impacts: excessive trash; stress on local water and sanitation systems; the need for more public bathrooms; traffic congestion; traffic-related threats to public safety; noise and disturbance of fragile local ecosystems; and parking challenges for visitors and locals alike. These impacts often exceed the capacity of existing infrastructure and local financial resources. As directed by the Coastal Act, the CCC needs to balance the laudable goal of preserving

public access against these impacts to ensure there is reasonable management of public access, financial resources for impacted communities to retain their special character, and attention to these consequences in connection with new development and other CCC policies.

Thus, in accordance with Coastal Act Section 30253€, we ask that an additional Objective be added to "Coastal Resources – Goal 3 – Protect and Enhance Coastal Resources":

> Objective 3.x Protect the Unique Character of Special Communities and Neighborhoods.
> 3.x.1 Update LCP guidance on protection of special communities and neighborhoods that, because of their unique characteristics, are popular visitor destination points for recreational uses.
> 3.x.2 Encourage sensible management solutions and sources of financial support where increased coastal tourism threatens environmental resources, the character of coastal communities, the financial ability of local agencies to serve tourist needs, and/or the visitor experience.
> 3.x.3 Outreach to coastal communities to promote information sharing on key issues relating to the management of increasing tourism through guidance documents, webinars, and/or workshops.

Like the protections of Objective 3.3 for agriculture (which served as a model for this proposed objective), this Objective would ensure that the CCC and its staff will address these issues protected under the Coastal Act and not otherwise mentioned in the draft Strategic Plan.
These issues are of such importance to our villages and others along the California Coast that they should also be mentioned in the Vision Statement. We propose this addition:

Our Vision:

> The California coast is available for all to enjoy through thousands of public accessways to and along the shoreline, a completed California Coastal Trail, a well-supported network of parks and open spaces, and a wide range of visitor-serving facilities, including lower-cost campgrounds, hostels, and hotels. The rich ecological diversity of the coast and ocean, including beaches, rocky shorelines, wetlands, riparian areas, and sensitive terrestrial habitats, is protected and thriving. Scenic rural landscapes are maintained, coastal agriculture is flourishing, the unique characteristics of the special communities and neighborhoods that attract coastal visitors are preserved, and cultural resources are protected...

Bolinas Public Utilities District

For the town of Bolinas, the Coastal Act's mandate to protect the special communities and neighborhoods in the coastal zone is of immense importance. In addition to ACMV's comment letter, we note that although Goal 4 in the Draft Plan

purports to "support resilient coastal communities", none of the listed objectives revolve entirely around the Commission's goals of preserving public beaches and enhancing visitor access to the beaches. Admirable as those goals are, we submit that the Commission also must focus attention on the fates of communities, including Bolinas, which front those beaches and attract coastal visitors. For example, an objective should be included in Goal 4 stating that the Commission will seek to help existing coastal communities survive in the face of projected rising sea levels. We acknowledge that this may require the Commission to balance competing provision of the Coastal Act, namely: the protection of beaches vs. the need to protect existing local communities as sea levels rise. Indeed, this is the exact sort of balancing of priorities envisioned by the Coastal Act. Another objective should be included to recognize the need to balance parking access for beach visitors with the protection of the beaches and residential neighborhoods located there. For example, Objective 2.2.3 should specifically include resident permit parking as a recommended option.

Muir Beach Community Services District

Visitors have always delighted in visiting the coastal towns and villages and now the popularity of this activity has only increased since the advent of social media. Historic visitors' interest and focus has continues to be on the coastal village experience for which 30253(e) was enacted to protect. But, with the increase in day-use and overnight visitors, comes the additional burden they put on existing water conservation efforts and supplies, trash collection and shoreline cleanup, finite septic capacities, parking limitations, traffic congestion, emergency services, and public safety.

The Coastal Commission needs to interpret the Coastal Act as the balanced document and ideal vision for which it was created, giving equal consideration to those parts of the Coastal Act that support public access to the coast, but without overburdening or endangering the coastal resources and natural environment beyond a reasonable carrying capacity.

East Shore Planning Group

Indeed, Marshall is a "poster child" for the purposes for which 30253(e) was enacted. Since the narrow-gauge railway from Sausalito opened in the 1870s, Marshall has been a Mecca for tourists seeking the coastal experience of boating, fishing, hunting and enjoyment of the natural beauty, as well as consuming oysters and other locally harvested seafood. The ranches along the shore produce the highest quality organic milk, livestock and cheeses for which the area is renown. The historic buildings, small boatyard and modest coast-side dwellings add to the ambience and character of Marshall and the entire area.

But the area's increasing popularity, as well as conditions imposed by the Coastal Commission and its staff in connection with coastal development permits, are very real threats to the community's viability for visitors and residents alike. So it is of vital importance to consider the protection of the coastal resources and the community

character of our villages along with the other resources that the Coastal Act protects, and that should be specified in the Strategic Plan.

District 4 Comments

I commend the Commission for adding Diversity, Equity, Environmental Justice, and Tribal Relations as their Goal 5. This goal and set of objectives are consistent with my priorities as District 4 Supervisor; however, I suggest that the Commission consider adding the following objectives:

5.x.1 Streamline permitting processes to increase and expand affordable housing opportunities for our workforce, service workers, emergency responders, rangers, etc.

5.x.2 Develop programs to diversify our coast through low-cost access options including affordable camping

Given the dire need for affordable housing in our Coastal zone, these objectives will help some of our most vulnerable community members. As well, as provide affordable opportunities for visitors from all backgrounds to visit our beaches. Our local economy and schools will ultimately benefit too. They also propel forward the Commission's **Objective 2.3 to Remove Barriers to Public Access and Develop Programs to Bring More People to the Coast.**

In closing, I congratulate the Commission for this Draft Strategic Plan for 2020-2025. It is evident that the California coast faces greater challenges today than ever before, but I look forward to partnering with our local Coastal Commission representatives to advance the goals and objectives presented in this plan.
Please feel free to contact me for additional information.

Respectfully,

Dennis Rodoni, District 4
Marin County Board of Supervisors

COUNTY OF MARIN

COMMUNITY DEVELOPMENT AGENCY
PLANNING DIVISION

Brian C. Crawford
DIRECTOR

Thomas Lai
ASSISTANT DIRECTOR

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February 12, 2020

California Coastal Commission
Executive Division
45 Fremont Street, Suite 2000
San Francisco, CA 94105

RE: **California Coastal Commission Strategic Plan 2020-2025**

Thank you for the opportunity to provide comments on the California Coastal Commission's 2020-2025 Strategic Plan. We have reviewed the document and support the Commission's goals and objectives for coastal protection. In particular, we appreciate the Commission's efforts to support resilient coastal communities in light of climate change impacts by educating and engaging with local communities, supporting development and implementation of adaptation projects, and collaborating with local governments on Local Coastal Plan updates.

We would also like to express our full support for suggestions contained in correspondence from the Alliance of Coastal Marin Villages (ACMV), which was sent to you under separate cover and is also provided as an attachment to this letter. The ACMV is a coalition of representatives from West Marin's ten villages which meets regularly to discuss issues of common concern. As noted in their letter, both the Coastal Act and Marin County's Local Coastal Plan support the protection of coastal communities that have become visitor destinations in their own right due to their special characteristics and incomparable settings. The impacts of increasing tourism on the character and infrastructure of these villages has been a long-standing concern. Accordingly, we concur with their recommendation to supplement the Strategic Plan goals and objectives related to Coastal Resources to recognize the impacts tourism can bring to coastal villages and the need to protect and preserve the unique character of these special communities in Marin and throughout the Coastal Zone.

In addition, the County of Marin is fully committed to equity in all its planning and actions. We strongly support Goal 5 for advancing diversity, equity, environmental justice, and tribal relations. We suggest you add one other objective in this regard - seeking to develop a better understanding of how those communities use our beaches and coastlines, identifying any impediments to that use, and developing ways to expand their opportunities.

Finally, we would request that guidance documents envisioned by the Strategic Plan be developed collaboratively with local communities to ensure that such guidance reflects community-specific factors and is practical, feasible, and enforceable at the local level, consistent with the explicit authority provided by the State Legislature and the Coastal Act.

Thank you for your consideration of these suggestions and we look forward to continuing our collaborative work with Commission staff during the remainder of Marin's Local Coastal Plan Update process.

Sincerely,

for

Brian C. Crawford
Director

Attachment: Alliance of Coastal Marin Villages letter, February 5, 2020

From:	Derek Dolfie
To:	Coastal Strategic Plan Comments
Subject:	League of California Cities Comment Letter - Coastal Commission Strategic Plan 11.04.20
Date:	Wednesday, November 4, 2020 4:19:57 PM
Attachments:	image003.png League of CA Cities - CCC 2021-2025 Strategic Plan Update Public Comment 11.4.20.pdf

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Hello,

Attached is the League's comment letter on the Coastal Commission's Proposed Final Draft of the 2021-2025 California Coastal Commission Strategic Plan. Please let me know if you have any questions. Thank you!

Best Regards,

Derek Dolfie
Legislative Representative
League of California Cities
Direct: 916-658-8218
ddolfie@cacities.org | www.cacities.org

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November 4, 2020

The California Coastal Commission
455 Market Street, Suite 300
San Francisco, CA 94105
Submitted Via Email: StrategicPlanComments@coastal.ca.gov

RE: Public Comment: Proposed Final Draft of the 2021-2025 California Coastal Commission Strategic Plan

Dear California Coastal Commissioners and Commission Staff,

The League of California Cities (League) appreciates the opportunity to provide comments on the California Coastal Commission's (Commission) Proposed Final Draft of the 2012-25 California Coastal Commission Strategic Plan (the "Plan"). For nearly fifty years, the Commission has been charged with implementing the Coastal Act. The Coastal Act requires higher standards for new development in the coastal zone and guarantees the right of coastal access for all.

The Commission has prepared the Plan, as required by the National Oceanic and Atmospheric Administration (NOAA), to prioritize the functions, programs, and processes that the Commission administers. The League is pleased this Plan includes measurable evaluation criteria that will be used to help the Commission and staff determine the effectiveness of the actions contained in the Plan. Additionally, the League appreciates the Commission's efforts to work with us (Objectives 6.1.6, and 8.1.1) and the Local Government Working Group to prepare the Joint Statement of Principles for Sea Level Rise Adaptation Planning. The League believes these efforts should continue to facilitate meaningful dialogs with local governments that result in successful policy platforms in the future.

While the Plan does identify actionable goals for the Commission to implement, there continues to be some concerns regarding the Commission's expansion of responsibilities and associated impacts to municipal achievement of state mandates. These issues are discussed in more detail below.

Role of the Coastal Commission
Over the years, the Coastal Act's clearly defined goals for the coastal zone in California have been interpreted to give the Commission the ability to address changing circumstances in an evolving world, as it should. However, the Plan adds additional tasks beyond the Coastal Act's core statutory authorization. For example, some items, such as Objective 4.3.5, that develop policy guidance for evaluating shoreline management options in light of sea level rise, are valuable ideas and worth exploring. However, some aspects of the Plan go beyond the text of the Coastal Act, which raises concerns.

The previous version of the Plan contained additional items, such as addressing sediment management, beach nourishment, shoreline armoring, sand retention, structures, and living shorelines. When these items were included in the previous Plan, we were concerned that such initiatives would have far reaching implications beyond the coastal zone, encroach on local jurisdictions developing Local Coastal Plans (LCPs), and could affect the economic needs of Californians. We are happy to see these items removed from the final Plan, but the concerns over how shoreline management adaptation options will

be implemented continue. Furthermore, if shoreline management continues to chip away decades of past practices for those with approved LCPs, it can significantly impact a city's future ability to achieve desired outcomes included in both local policy documents and the Coastal Act.

Additionally, we understand the fiscal challenges the Commission is facing and recognize its staffing challenges. Cities, too, are in the same situation, with budgets severely impacted by COVID-19. However, cities are experiencing delays to important public infrastructure and private projects, and local regulatory efforts due to understaffing at the Commission. This places a drain on local communities attempting to comply with ever increasing mandates by other state agencies. In this time of budgetary uncertainty, we find it prudent to advocate that all parties have the resources to carry out their missions to help their constituencies before they take on additional responsibilities.

Lastly, cities want to work with the Commission but find it challenging when the Commission takes on new responsibilities outside of the legislative or regulatory process. We agree with the Commission's core value that "maximum public participation" is critical in the functioning of the Commission and would urge the Commission to work closely with the cities on the coast to achieve their goals. If more responsibilities are desired, that are not expressly granted to the Commission, we urge those proposals go through the established legislative and regulatory processes in California that afford cities the opportunity to comment.

<u>Recommendations:</u>

- Continue focusing Commission staffing efforts on items clearly under the purview of the Commission and maintain local community discretion when approved LCPs exist; and
- Changes to the scope of responsibilities for the Commission should be sought from the electorate through existing legislative and regulatory processes.

Competing State Mandates

The Plan acknowledges the duties and responsibilities of the Commission have changed since the Coastal Act was passed by the Legislature in 1976. Cities, as well, have seen their roles and responsibilities change as cities are being placed under ever increasing pressure to address the State's housing crisis, reduce vehicle miles traveled (VMT), and eliminate greenhouse gas emissions (GHGs). Cities understand and support these issues, as they are severely affected by high costs of living, congestion, and sea level rise. Cities are also, however, exceedingly challenged in these areas as they are required to balance mandates by different state agencies with the standards of the Commission.

Addressing the housing crisis is of particular importance to cities in the coastal zone. The Commission has also expressed interest in helping spur affordable housing construction. To accomplish this effectively, the League urges the Commission to work with the Department of Housing and Community Development (HCD) to coordinate the missions of these two entities. This includes clarifying Commission standards that have long been at odds with the ability for coastal communities to provide all forms of housing, but especially affordable housing. Such items include, but are not limited to, viewshed protection issues, height limitations for development, elimination of parking requirements for specific housing types, and housing densities and type. The Commission is making efforts in this regard, as evidenced by recent approvals of Accessory Dwelling Unit ordinances by several cities and counties.

Continuing to enhance the local jurisdiction's ability to aid in the creation of new housing of varying styles, densities, and prices would further help address the issue of reducing VMT, allowing people more opportunity to live in the communities in which they work. Reducing VMT will also reduce the release of GHGs, which will aid the Commission and cities in addressing climate change, such as sea level rise.

Recommendations:

- The Commission work with HCD to develop clear standards for coastal communities to provide affordable housing, as required by both the state and the Coastal Act; and
- The Commission aid cities to work toward ensuring those that work on the coast can also live on the coast.

Lastly, the League requests the Commission defer to the elected officials of a city with respect to choices in the implementation of a LCP that complies with the requirements of state law and regulation. As you know, cities are not all the same and thus often require different solutions to solve coastal issues.

Thank you for the opportunity to provide comments and for your consideration. We look forward to continuing to work with you and the Commission staff on the important work of fostering and protecting California's coast. If you have any questions, do not hesitate to contact me via email at ddolfie@cacities.org.

Sincerely,

Derek Dolfie
Legislative Representative

From:	Katherine Biala
To:	Coastal Strategic Plan Comments
Subject:	Fwd: Public Comments related to the EJ section of the CCC Strategic Plan
Date:	Wednesday, November 4, 2020 4:57:41 PM
Attachments:	K Biala Public Comment on CCC Strategic Plan.docx

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Kathy Biala
kybiala@icloud.com
cell: 831-242-0023
Mailing address: 3012 Crescent St.
Marina, CA 93933

Begin forwarded message:

From: Katherine Biala <kybiala@icloud.com>
Subject: Public Comments related to the EJ section of the CCC Strategic Plan
Date: November 4, 2020 at 4:56:44 PM PST
To: Noaki Schwartz <Noaki.Schwartz@coastal.ca.gov>, StrategicPlanComments@costal.ca.gov

Noaki and staff,

Attached are my public comments. Thank you for your diligence in creating a detailed and thoughtful document!

Cordially,
Kathy Biala

Kathy Biala
kybiala@icloud.com
cell: 831-242-0023
Mailing address: 3012 Crescent St.
Marina, CA 93933

To: CA Coastal Commission
From: Kathy Biala, resident of Marina, CA
Date: Nov. 4, 2020
Re: Strategic Plan Public Comments

Dear CA Coastal Commission staff and Commissioners,

I have enormous respect for this document as it relates to the Goal 5 Evaluation Criteria in considering environmental justice and equity issues. In our recent hearings on the CalAm desalination project in which the staff recommended twice to deny the project, based in part, on the environmental injustices to a disadvantaged community of color, the commission demonstrated determination to objectively evaluate this project based on the new EJ policies.

But environmental injustice determinations go beyond the mere staff evaluation weighed against an EJ policy. It requires the tools that can objectively and factually determine the presence of EJ, as you have so skillfully done, and part of this means fact finding of the perceptions and the lived experiences of those directly affected. The CCC also gave special attention to and made concerted efforts in this regard in Marina's case. Then more broadly, the CCC strategic plan attempts to ensure that LCPs in general also incorporate these new standards. Further, your strategic plan attempts to ensure that the CCC staff body itself promotes equity and inclusion through hiring and retention practices. If staff is to assess and write reports evaluating the existence of environmental justice on applicant projects, it stands to reason that the staff itself must also value equity and inclusion by hiring and maintaining staff who understand and value the person of color perspective.

Of all of these criteria, I want to emphasize 5.53 and 5.5.4 that includes training for the ***commissioners***. I am so pleased that you have identified this in your plan. As I have been so personally involved with the CalAm project over several years now, and am deeply grateful to the staff for their strong adherence to the principles of EJ, it is now a great unknown whether the appointed commissioners' value or fundamentally support the new EJ policy. Systemic racism can easily be ignored and project applications approved on a multitude of many other complex and "justifiable" reasons that would essentially ignore and re-prioritize the larger picture of essential environmental injustices. Ultimately, if the commissioners hold the final authority in denying or approving a project, without knowing their biases or lack of acceptance of the concept of EJ, nothing that affected communities or staff reports can say, would ultimately prevail when commissioner votes are counted. Therefore, the quality and the intensity of training of commissioners, to me, is of the utmost importance and this, of course, is quite the challenge since they are political appointees. This will be your greatest obstacle, I believe, but one that is so critical to communities of color since intolerant or biased or even prejudiced commissioners can by their vote, nullify the staff's recommendations related to EJ.

I just wanted to commend the CCC for this section on EJ and to reinforce that you have encapsulated all the relevant and critical pieces to ensure to the best of your abilities, that exploitation of communities of color will not occur .

Thank you very much.

Kathy Biala

From: **Jana Zimmer** <zimmerccc@gmail.com>
Date: Sat, Oct 31, 2020 at 1:42 PM
Subject: Comment for Nov. 6 Item 5- PLEASE DISTRIBUTE
To: John Ainsworth <jainsworth@coastal.ca.gov>
Cc: Cortney S. Warren, PhD, ABPP <cwfishkin@gmail.com>, Lisa Weinberg <lweinberg@gaineslaw.com>, John Flynn <jflynn@nossaman.com>

Jana Zimmer
Attorney/Governmental Relations Consulting
2640 Las Encinas Lane
Santa Barbara, CA. 93105
(805) 705-3784
e-mail:zimmerccc@gmail.com

October 30, 2020

Honorable Stephen Padilla, Chair
California Coastal Commission
45 Fremont Street
San Francisco, CA.

By: e mail

Re: **Agenda Item #5 November 6, 2020 Strategic Plan**

Dear Chair Padilla and Honorable Commissioners:

I am writing to provide comment on your staff's recommendations regarding **Enforcement, Section G.,** of the draft Strategic Plan. As some of you may remember, I served on the Commission from 2011-2015. I voted to support Sen. Atkins' bill establishing the authority for the Commission to seek administrative penalties, when it was being debated in 2013-2014. In so doing, I gave little attention to warnings from advocates for property owners that this power could be abused, because I had complete faith that your staff would use their new authority judiciously and guarantee that your Commission's decisions and process would be fundamentally fair to the accused.

Since the end of my term, I have limited my involvement in Coastal Commission matters to cases which I believed could best be resolved through negotiation, rather than litigation. My experience in two, recent enforcement matters has convinced me that the Commission's current regulations and process in administrative penalty proceedings are simply inadequate. Therefore, I am most concerned with the recommendation in Section 7.1.1 to "**Expand administrative penalty authority beyond public access to the remainder of the program and identify other potential legislative changes to strengthen the enforcement program.**" The process needs substantial improvement *before* the Commission seeks expansion of its authority. And, the Commission enforcement staff needs to prioritize its efforts and focus its resources on permits that the Commission itself has approved, rather than

attempt to direct local government to reinterpret permits the Commission had nothing whatever to do with approving, and staff has no administrative competence to interpret.

I am currently representing an individual homeowner who is being threatened with massive penalties, which exceed the value of her home, for **a violation that a reviewing court will determine simply does not exist,** as a matter of law. She is being pressured to "consent" to a physical solution that the law does not authorize the Commission to require. She needs a final decision from the Commission before she can seek judicial review of what is almost certain to be an outrageous staff recommendation, based on their handling of the matter to date. In the current hearing process:

- She cannot obtain all relevant records because your staff is claiming they are exempt from disclosure;
- She cannot subpoena evidence or witnesses;
- She does not have the right to cross- examine witnesses;
- There are no rules of evidence;
- Staff presents their opinion and conclusions without producing their experts to testify;
- She is required to submit Declarations under penalty of perjury,* but staff and their witnesses are not required to testify under oath;
- Staff controls the flow of documents and evidence presented, requiring the accused to make their case first, thereby misallocating the burden of producing evidence;
- Staff controls the flow of rebuttal evidence;
- Staff will suggest that you accept their interpretation of documents they have no administrative competence to interpret;
- Staff asserts jurisdiction to enforce a local permit that the Commission did not approve, on a property where the Commission has never sought to review local permits, in thirty years, and where the local government never requested that the Commission "assume" jurisdiction against my client;
- Local government in this case has an administrative procedure that (1) provides for a hearing *before* penalties are considered (2) includes prospective penalties only, (while Commission staff asserts that penalties can accrue prior to a hearing up to five years at $11,250 per day;(3) and the local decision is directly reviewable by the Superior Court, under a "de novo" standard of review. Despite its workload, staff is holding on to "jurisdiction" it never lawfully acquired over this project for the sole purpose of coercing my client to agree to an outcome the courts would never uphold.

*I am attaching here, for illustrative purposes, my client's Declaration under Penalty of Perjury, submitted with her Statement of Defense on October 1, 2020 as Exhibit 75 thereto. Notwithstanding the clear requirements of Section 30812(c) of the Coastal Act to provide a hearing at the first Commission meeting for which legal notice can be given, staff has not scheduled a hearing on this matter, nor told us when they might do so. Meantime, staff contends that the accused violator should be liable for penalties retroactive to the date that their Notice of Violation was delivered.

The current regulations simply do not assure the due process rights of the accused. Instead of seeking legislative changes to expand its authority, the Commission should seek independent, third-

party review of the fairness and efficacy of the current system. Then, staff should draft, seek approval from the Office of Administrative Law, and implement regulations to govern your administrative proceedings under Section 30821 which (1) assure that the due process rights of the accused are adequately protected in the hearing process; (2) clarify the Commission's authority to assume jurisdiction over the enforcement of local permits to only those cases where the local governing body adopts a formal resolution requesting you to do so; and (3) where "correction" of an alleged violation requires a coastal development permit to be considered by the Commission, assure that the enforcement staff does not impermissibly blur the boundary between permitting and enforcement by "strategizing" with permit staff over outcomes.

Unless and until these procedural safeguards are implemented, the **only** Legislative change that should be requested is a clarification that judicial review of decisions under Section 30821 is "de novo", as it is under Gov Code 53096.4, and as was represented to the Commission when we were asked to support the Atkins bill.

Thank you for your consideration of these concerns.

Very Truly Yours,

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