



January 29, 2019

Veronica Dutch
OPP Docket
Environmental Protection Agency Docket Center (EPA/DC)
(28221T)
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

Subject: Amitraz – Preliminary Ecological Risk Assessment and Endangered Species Assessment for Registration Review of the Conventional Use in Honey Bee Hives (EPA-HQ-OPP-2009-1015)

Dear Ms. Dutch:

On behalf of the Bay Area Clean Water Agencies (BACWA), we thank you for the opportunity to comment on the Preliminary Ecological Risk Assessment (ERA) for amitraz. BACWA's members include 55 publicly owned wastewater treatment facilities ("POTWs") and sewer collection system agencies serving 7.1 million San Francisco Bay Area residents. We take our responsibilities for safeguarding receiving waters seriously. BACWA is especially interested in pesticides that are used in manners that have transport pathways to the sanitary sewer, as even the most sophisticated wastewater treatment plants cannot fully remove complex chemicals like pesticides.

Every day, BACWA members treat millions of gallons of wastewater that is then discharged to fresh or salt water bodies, including local creeks and rivers, bays, and the Pacific Ocean. These waterways provide crucial habitat to a wide array of aquatic species and waterfowl. In some cases, waters receiving POTW discharges ("receiving waters") may be effluent-dominated in that there is little to no dilution, either because the receiving water is small or there is a lack of mixing at certain times due to thermal or saline stratification.

BACWA has a strong interest in amitraz due to the existence of indoor uses and the associated pathway to sanitary sewers. The primary purpose of this letter is to request that EPA conduct a Preliminary Ecological Risk Assessment for amitraz that incorporates the latest available aquatic invertebrate toxicity data as well as an evaluation of sewer discharges from pet products. Several studies¹, including a recent study involving several of our member agencies, suggest that pet flea/tick control products have a direct pathway, via sewer collection systems, to POTWs. While these studies have focused on pet spot-on products applied directly to pet fur, they prove the existence of the pathway for pesticides in pet collars – which release pesticides onto pet fur – to subsequently be transported to POTWs.

¹ See Appendix 1 and enclosures

BACWA appreciates that OPP has started to conduct evaluation of risks associated with pesticide discharges to the sewer system (“down the drain” risk assessments). Omitting evaluation of the sewer discharge environmental exposure pathway can be harmful to the environment and prove costly for POTWs, as detailed below.

In almost every U.S. state – including California – state law precludes any local regulation of pesticide sales or use. As we have no local option to control use of pesticides consumer products, it is essential to us that OPP’s Preliminary ERA adequately evaluates potential impacts to wastewater quality, and results in mitigation measures ensuring that impacts to the beneficial uses of the receiving water are *prevented*.

For these reasons, it is of utmost importance to BACWA that all pet flea/tick control products be carefully and thoroughly evaluated.

In addition to commenting on the Preliminary ERA, we are also taking this opportunity to provide input on possible mitigation strategies for EPA to discuss with amitraz registrants. We are providing this input at this time because mitigation measures may be necessary and we understand that the next opportunity for public comment will be after such discussions and after EPA has prepared its proposed decision.

Thank you for this opportunity to present our input on each of these topics.

Background – Pesticide discharges to the sewer can harm the environment and be costly

Pesticide discharges to the sewer system can prove costly for POTWs, due to the potential for pesticides to cause or contribute to wastewater treatment process interference, NPDES permit compliance issues, adverse impacts to receiving waters, degradation of recycled water quality and/or ability to reuse biosolids, in addition to exposing POTWs to the potential for third party lawsuits under the Federal Clean Water Act (CWA).

Of particular concern is the ability of a specific pesticide to cause exceedance of a POTW’s effluent toxicity limits. One universal water quality standard in the U.S., which stems directly from the CWA, is that surface waters cannot be toxic to aquatic life. NPDES permits require POTWs to demonstrate that they meet this standard by evaluating acute and chronic toxicity using EPA standard methods (set forth in 40 CFR Part 136). To evaluate toxicity, every POTW must (1) conduct toxicity screening tests with a range of species, (2) select the most sensitive species, and (3) perform routine monitoring (typically monthly or quarterly). These monitoring data are used to determine whether the discharger has a *reasonable potential* to cause or contribute to toxicity in the receiving water. If it does, the CWA requires that numeric effluent limits be imposed, otherwise POTWs may be given numeric effluent triggers for further action. In the event that routine monitoring *does exceed* a toxicity limit or trigger, the POTW must perform accelerated monitoring (e.g., monthly); and if there is still evidence of consistent toxicity, the discharger must do a Toxicity Reduction Evaluation (TRE) to get back into compliance. The TRE requires dischargers to evaluate options to optimize their POTWs and conduct a Toxicity Identification Evaluation (TIE), the cost of which can vary from \$10,000 to well over \$100,000 depending on complexity and persistence of the toxicant. The goal of the TIE

is to identify the substance or combination of substances causing the observed toxicity. If a POTW's effluent is toxic because of a pesticide, it may not have any practical means to comply with CWA-mandated toxicity permit limits.

Once identified, the cost to treat or remove the toxicity causing compound(s) can vary dramatically. Often, there are few ways for a discharger to mitigate the problem other than extremely costly treatment plant upgrades. Upgrading POTWs is often ineffective for organic chemicals like pesticides that appear at sub microgram per liter concentrations, largely because sewage is a complex mixture of natural organic compounds. Regardless of this, the discharger must comply with its CWA permit limits. If a discharger violates a toxicity limit, it can be subject to significant penalties (in California up to \$10/gallon or \$10,000 per day).

In addition, when surface water bodies become impaired by pesticides, wastewater facilities may be subject to additional requirements established as part of Total Maximum Daily Loads (TMDLs) set for the water bodies by EPA and state water quality regulatory agencies. A number of pesticide-related TMDLs have been adopted or are in preparation in California. The cost to wastewater facilities and other dischargers to comply with TMDLs can be up to millions of dollars per water body per pollutant. This process will continue as long as pesticides are approved for uses that result in water quality impacts; it is therefore imperative that EPA conducts a Preliminary ERA focusing on water quality impacts and for EPA to take action to ensure that any impacts are prevented or fully mitigated.

BACWA requests that OPP conduct a Preliminary Ecological Risk Assessment that includes an evaluation of sewer discharges from amitraz pet tick control treatments

BACWA is concerned that risks associated with indoor amitraz use were not examined and respectfully asks the EPA to include this analysis (a "down-the-drain" risk assessment) in the revised assessment. EPA has POTW predictive modeling tools which are suitable for conducting this assessment and has conducted similar assessments for many other pesticides.

We request that EPA specifically analyze sewer discharge for pet flea/tick collars.

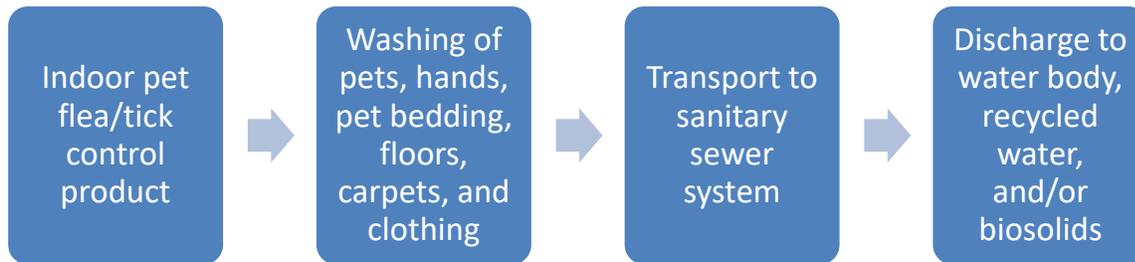
As the amitraz human health risk assessment² explains, pesticides in pet flea/tick collars are released as either particles or liquid onto the pet's fur. Davis et al. quantified transfer of tetrachlorvinphos from pet collars onto the gloved hands of subjects interacting with the collared pet.³ Similar transfer also occurs for amitraz, as documented by a study cited in the human health risk assessment.⁴ Once the pesticide has transferred onto the pet's fur, human hands, and other indoor surfaces, it is available for further transfer to the sewer system, as explained in Appendix 1. Pet flea/tick control chemicals are transported within a home to an indoor drain that flows to a POTW via the pathways illustrated in Figure 1.

² US EPA Office of Pesticide Programs (2018). Amitraz. Draft Human Health Risk Assessment for Registration Review. Memorandum D435892.

³ Davis, M., et al. (2008). "Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos," *J. of Exposure Science and Environ. Epidemiology* **18**:564-570.

⁴ Memo, A. Gavelek, D424229, 9/30/2015. "Determination of Transferable Residues of Amitraz from the Hair of Dogs Following the Application of the Preventic® Collar (Formulated End-Use Product 516.20)" MRID 49468801.

Figure 1. Amitraz Pathway: From Pet Treatments to Wastewater Discharge



Scientific studies detailed in Appendix 1 examined the pathways that transport pet flea/tick active ingredients from pet fur to the sewer system, both directly (through dog washing) and indirectly (such as after transfer onto human hands, socks, or clothing that are subsequently washed). Based on the data from these studies and pet population data, it is clear that pet flea/tick control products are significant sources of pesticides to POTWs that should be accounted for in the Preliminary ERA.

The Preliminary ERA was limited to evaluation of the use of amitraz in bee hives. The ERA should be expanded to evaluate sewer discharges from pet treatments—including analysis of the latest available aquatic invertebrate toxicity data—given that amitraz has pathways to POTWs and surface waters.

BACWA requests that EPA consider risk mitigation for amitraz

Given findings for other pet flea/tick control products, the “down-the-drain” risk assessment for amitraz may conclude that risk mitigation is warranted to reduce POTW amitraz discharges and associated invertebrate toxicity. Because 100 percent of POTWs must comply with the Federal Clean Water Act 100 percent of the time, whenever EPA identifies significant risks from pesticides discharged to POTWs, BACWA believes that a robust exploration of risk mitigation is imperative.

In response to the finding that pet flea/tick control products are major sources of pesticides to POTWs, BACWA completed an assessment of pet flea/tick control alternatives. Although it focused on flea products, this assessment also highlighted several practical oral alternatives that are also effective on ticks.

In light of these findings, BACWA requests that OPP conduct its risk-benefit evaluation for pet flea/tick control products as a group (i.e., considering fipronil, imidacloprid, indoxacarb, and pyrethroids, which are also undergoing Registration Review) and in the context of the broad range of available non-pesticide alternatives, including FDA-approved oral medications.

While we agree that pet flea/tick control has societal benefits, our review of control options detailed in Appendix 2 identified many alternatives that are likely far less environmentally problematic than on-pet or indoor pesticide treatments. For example, the new generation of FDA-approved orals seems to be more convenient, equally or more effective, and well accepted

by pet owners and veterinarians. Finally, we emphasize that we do not believe that fipronil, imidacloprid, indoxacarb, or pyrethroids are acceptable alternatives to amitraz.

BACWA suggests that EPA consider the following additional risk mitigation strategies for indoor amitraz products:

- Determine the minimum application rate (i.e., collar material concentration) necessary to achieve tick control. This would eliminate unnecessary overuse and minimize POTW discharge quantities.
- Consider adding wastewater-protective use restrictions to product labels—such as dissuading pet owners from washing their pets with the collar on.

Thank you for the opportunity to provide this feedback regarding both the Preliminary ERA and subsequent mitigation strategies. We ask that OPP evaluate amitraz discharges to POTWs and the subsequent potential impacts to effluent toxicity and explore mitigation options. BACWA requests that EPA coordinate with the California Department of Pesticide Regulation (CDPR) (which has extensive relevant information and expertise), veterinarians, and registrants; and bring in the latest scientific information – including CDPR scientific studies and modeling that are currently underway.

If you have any questions, please contact BACWA's Project Managers:

Karin North
City of Palo Alto
(650) 329-2104

Karin.north@cityofpaloalto.org

Autumn Cleave
Wastewater Enterprise, San Francisco Public Utilities
(415) 695-7336

ACleave@sfwater.org

Respectfully Submitted,



David R. Williams, P.E.
Executive Director
Bay Area Clean Water Agencies

Enclosures:

1. Sadaria, A.M. et al. 2017. Passage of Fiproles and Imidacloprid from Urban Pest Control Uses Through Wastewater Treatment Plants in Northern California. *Environmental Toxicology and Chemistry*. 36 (6), 1473-1482.
2. Bigelow Dyk, M. et al. (2012). Fate and distribution of fipronil on companion animals and in their indoor residences following spot-on flea treatments, *Journal of Environmental Science and Health, Part B: Pesticides, Food Contaminants, and Agricultural Wastes*, 47(10): 913-924
3. Teerlink, J., J. Hernandez, R. Budd. 2017. Fipronil washoff to municipal wastewater from

dogs treated with spot-on products. Sci Total Environ 599-600: 960-966.

cc: Yu-Ting Guilaran, Director, Pesticide Re-Evaluation Division
Tracy Perry, EPA OPP Pesticide Re-Evaluation Division
Rick P. Keigwin, Jr., Director, EPA OPP
Andrew Sawyers, Director, EPA Office of Water, Office of Wastewater Management
Tomas Torres, Director, Water Division, EPA Region 9
Frank T. Farruggia, Environmental Risk Branch 1
Sujatha Sankula, Environmental Risk Branch 1
Greg Orrick, Environmental Risk Branch 1
Mark Baldwin, Chemical Review Manager, Risk Management and Implementation Branch 5
Melanie Biscoe, Team Leader, Risk Management and Implementation Branch 5
Linda Arrington, Branch Chief, Risk Management and Implementation Branch 5
Marietta Echeverria, Director, Environmental Fate and Effects Division
Debra Denton, EPA Region 9
Patti TenBrook, EPA Region 9
Karen Mogus, California State Water Resources Control Board
Philip Crader, California State Water Resources Control Board
Paul Hann, California State Water Resources Control Board
Jodi Pontureri, California State Water Resources Control Board
Tom Mumley, California Regional Water Quality Control Board, San Francisco Bay Region
Janet O'Hara, California Regional Water Quality Control Board, San Francisco Bay Region
Rene Leclerc, California Regional Water Quality Control Board, San Francisco Bay Region
James Parrish, California Regional Water Quality Control Board, SF Bay Region
Debbie Phan, California Regional Water Quality Control Board, SF Bay Region
Jennifer Teerlink, California Department of Pesticide Regulation
Chris Hornback, Chief Technical Officer, National Association of Clean Water Agencies
Cynthia Finley, Director, Regulatory Affairs, National Association of Clean Water Agencies
Kelly D. Moran, Urban Pesticides Pollution Prevention Partnership
BACWA Executive Board
BACWA Pesticides Workgroup

Appendix 1

Pet Pesticide Treatments: Evidence for the Pathway to the Sewer

Part I – Evidence for the Pathway to the Sewer

There is mounting evidence that pesticides from on-pet products (spot-ons and collars) and indoor foggers and sprays have exposure pathways to the sewer. The research summary below is organized first by the consumer use, followed by specific studies throughout a sewer collection system and at POTWs.

Topical Pet Flea/Tick Control Products - Background

Pet topical treatments are designed to impact one or more stages of the flea cycle through direct contact with the pesticide (rather than an adult flea biting the pet and obtaining the pesticide systemically with the consumed blood). Therefore, pesticides in topicals are not meant to enter the pet's bloodstream but rather are meant to stay on the pet's fur in order to be effective.

Pet Washing Discharge Pathway

Pet washing is likely a major discharge pathway for pet products. A study by California Department of Pesticide Regulation (CDPR) (Teerlink et al. 2017; enclosed)⁵ measured the washoff of fipronil spot-on products when bathing treated dogs. Fipronil was detected in all samples – even those collected 28 days post-application. According to the authors of the study:

“Results confirm a direct pathway of pesticides to municipal wastewater through the use of spot-on products on dogs and subsequent bathing by either professional groomers or by pet owners in the home. Comparisons of mass loading calculated using California sales data and recent wastewater monitoring results suggest fipronil-containing spot-on products are a potentially important source of fipronil to wastewater treatment systems in California. This study highlights the potential for other active ingredients (i.e., bifenthrin, permethrin, etofenprox, imidacloprid) contained in spot-on and other pet products (i.e., shampoos, sprays) to enter wastewater catchments through bathing activities, posing a potential risk to the aquatic organisms downstream of wastewater discharge.”⁶

Indirect Sewer Discharge Pathways

Several scientific studies have examined the transport of active ingredients from pet products onto surfaces, such as human hands, that are subsequently washed, completing a transfer pathway to the sewer system.

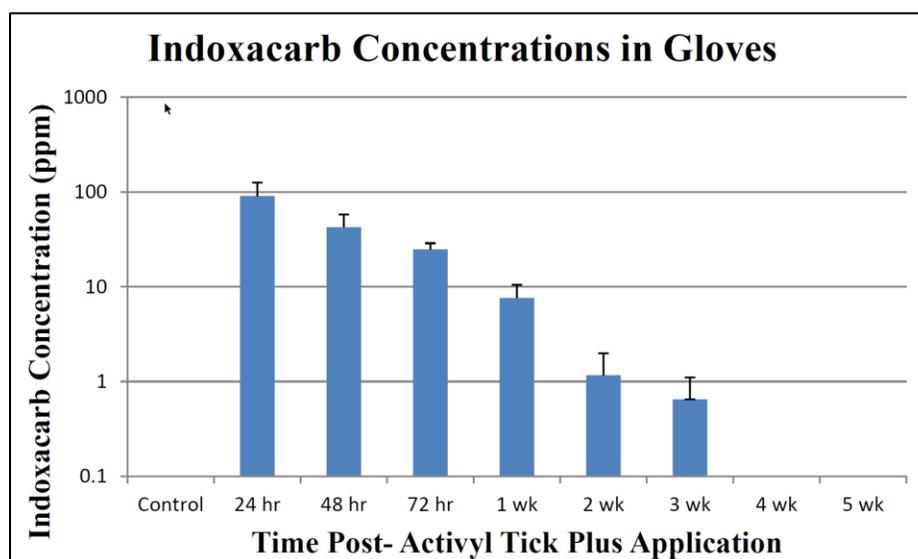
- *Spot-on treatment product to glove (hands) pathway*: A 2015 study by Litchfield et al. evaluated the transfer of permethrin and indoxacarb from a topical pet flea control

⁵ Teerlink, J., J Hernandez, R Budd. 2017. Fipronil washoff to municipal wastewater from dogs treated with spot-on products. *Sci Total Environ* 599-600: 960-966.

⁶ Teerlink, J., J Hernandez, R Budd. 2017. Fipronil washoff to municipal wastewater from dogs treated with spot-on products. *Sci Total Environ* 599-600: 960-966.

treatment to people's hands.⁷ In the study, the topical treatment was applied to dogs that had not received a topical treatment for at least two months. To simulate human exposure to the pesticides, "Glove sampling included the wipe sampling technique, which consisted of petting the dog forward and back along its back and sides, while avoiding the application site, for five minutes while wearing a 100% cotton glove." The cotton glove samples were collected at days 0, 1, 2, 3, 7, 14, 21, 28, and 35. While the results showed that the largest mass of indoxacarb was transported within the first week, there continued to be measurable transfer to the gloves, even at day 21. The study did not measure indoxacarb degradates, which likely formed during the study period.

Figure 2. (from Litchfield et. al. 2015) Indoxacarb concentrations in gloves after petting dogs who had application of indoxacarb ("Activyl Tick Plus") spot-on flea control (µg/L)



- *Spot-on treatment product to glove (hands) pathway:* A 2012 study by Bigelow Dyk et al. presents additional evidence of transport of a pet flea control product onto human hands and through homes.⁸ In the study, researchers monitored transfer of fipronil (from a commercially available spot-on product) onto pet owners' hands and within their homes over a four-week period following spot treatment application. Participants used cotton gloves to pet their dog or cat for 2 minutes at a time at specific intervals after the application (24 hours, 1 week, 2 weeks, 3 weeks, and 4 weeks). Participants also wore cotton socks for 2 hours a night for 7 nights in a row, for four consecutive weeks following application. The gloves, socks, and brushed pet hair were subsequently analyzed for fipronil and its degradates. Bigelow Dyk and colleagues also incorporated a

⁷ Litchfield et al., "Safety Evaluation of Permethrin and Indoxacarb in Dogs Topically Exposed to Activyl® Tick Plus," J Veterinar Sci Technology 2015, 6:2 <http://dx.doi.org/10.4172/2157-7579.1000218>. (enclosed)

⁸ Bigelow Dyk, M., et al. (2012) Fate and distribution of fipronil on companion animals and in their indoor residences following spot-on flea treatments, Journal of Environmental Science and Health, Part B: Pesticides, Food Contaminants, and Agricultural Wastes, 47(10): 913-924

fluorescent dye into the spot treatment to provide photographic evidence of spot-on pesticide transfer. The photographic results shown in the paper illustrate the transfer from the application location to other areas of the pet's fur and onto the pet owners' hands.

- *Pet collar to glove (hands) pathway*: One such study by Davis et al. quantified glove transfer of tetrachlorvinphos from pet collars.⁹ We understand that the U.S. EPA team reviewing tetrachlorvinphos (EPA-HQ-OPP-2008-0316) has examined this paper and is planning to use the glove residue data following feedback from the U.S. EPA's Human Subjects Review Board.⁷
- *In-house fogger and spray pathway*: A UC Riverside study from 2010 sought to better understand the human health consequences of indoor insecticidal treatments, comparing a fogger, a perimeter spray, and both crack-and-crevice sprays, and spot sprays.¹⁰ Researchers selected registered commercial products and applied per label instructions in rooms of unoccupied homes. They then evaluated the deposition of active ingredients, which included permethrin, chlorpyrifos, cyfluthrin, cypermethrin, and deltamethrin. They found that:

"Each application type produced a surface residue, but the residues differed sharply in deposition and distribution. Relative to the general distribution of residue following fogger applications, perimeter, crack-and-crevice, and spot applications resulted in less total chemical residue and limited distribution to within 0–40 cm of the wall."

"...fogger applications differ from all other methods of application that rely on directed sprays examined in this paper. This supports our proposal that deposition and spatial distribution are principally determined by the type of pesticide application (i.e. fogger vs. crack-and-crevice) and the actions of the applicator (i.e. heavy vs. light applications)."

In 1990, the California Department of Food and Agriculture published a dermal contact study presenting findings regarding the transfer of residue to people and their clothing following a chlorpyrifos/allethrin fogger treatment in carpeted rooms.¹¹ The rooms were all located in a new hotel so as to eliminate background pesticide residue and to provide repeatability from room to room. The foggers were set up per label instructions and were activated for two hours followed by ventilation of the room. Male and female participants later conducted a standardized exercise routine in specific locations in the room. Shirts, tights, gloves and socks were subsequently collected for analysis. Both allethrin and chlorpyrifos were detected in all exposed samples exceeding the minimum detection limits. Had these garments been placed in the laundry, this would have resulted

⁹ Davis, M., et al. (2008). "Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos," *J. of Exposure Science and Environ. Epidemiology* **18**:564-570.

¹⁰ Keenan, James J., John H. Ross, Vincent Sell, Helen M. Vega, Robert I. Krieger, "Deposition and spatial distribution of insecticides following fogger, perimeter sprays, spot sprays, and crack-and-crevice applications for treatment and control of indoor pests," *Regulatory Toxicology and Pharmacology* 58 (2010) 189–195.

¹¹ Ross, J., T. Thongsinthusak, H.R. Fong, S. Margetich, R. Krieger, California Department of Food and Agriculture, "Measuring Potential Dermal Transfer of Surface Pesticide Residue Generated from Indoor Fogger Use: An Interim Report," *Chemosphere*, Vol.20, Nos.3/4, pp 349-360, 1990.

in discharge to the sewer. Similarly, when the volunteer participants showered, the residue on their heads and other bare skin transferred to the sewer.

Based on the data from these studies characterizing pet-applied active ingredient transfer to owners' hands and the transfer of fogger active ingredients to room occupants, it appears that washing of hands, clothing, carpets and floors could be significant sources of pesticides to POTWs.

Evidence from Collection Systems

CDPR is in the process of completing a collection system ("sewershed") study within the City of Palo Alto's Regional Water Quality Control Plant.¹² The study involved twenty-four hour time weighted composite samples (influent, effluent, and ten sites in the collection system). Samples were collected from several discharge-specific sites with potential for relatively large mass flux of pesticides (i.e., discharges from pet grooming operation, pest control operator, and a laundromat). The samples were analyzed for a suite of pesticides. Preliminary results from the pet-grooming site provide evidence that pet washing is a pathway for pesticide discharges to sewer systems.

We encourage OPP to obtain the final results of this study, which should be available within the timeframe of OPP's exploration of mitigation strategies for amitraz.

POTW Influent and Effluent

Lastly, further insights regarding transport of indoor flea control products to POTWs comes from a study of fipronil and imidacloprid at eight POTWs that was recently conducted by the San Francisco Bay Regional Monitoring Program in collaboration with BACWA, CDPR and Arizona State University.¹³ The study monitored imidacloprid and fipronil, as well as its degradates, in the influent and effluent of eight urban California POTWs. The results indicated that fipronil, its degradates, and imidacloprid were ubiquitous in the influent sewage and final treated effluent of all eight participating POTWs, and – based on a detailed analysis of the sewer discharge sources of these two chemicals, which have relatively little indoor use other than pet flea control – provide compelling evidence that pet products may be the primary source of both chemicals in wastewater.

¹² See http://www.cdpr.ca.gov/docs/emon/surfwtr/presentations/presentation_130_targeted.pdf

¹³ Sadaria, A.M., Sutton, R., Moran, K.D., Teerlink, J., Brown, J.V., Halden, R.U., 2017. Passage of fiproles and imidacloprid from urban pest control uses through wastewater treatment plants in northern California, USA. Environ. Toxicol. Chem. 36:6 1473-1482.

Appendix 2: List of Currently Available Oral Pet Treatments for Fleas and Ticks (Alphabetical)

Active Ingredient	Example Product Names and Manufacturers	Dogs, Cats or Both?	Flea, Tick, Both	Dose Schedule	Adulticide?	Insect Growth Regulator?	Chemical Family	Year Registered
Afoxolaner	Nexgard (Merial)	Dogs only	Both	1 month	X	No	Isoxazoline ¹⁴	2013
Fluralaner	Bravecto (Merck)	Dogs only	Both	2-3 months	X	No	Isoxazoline	2014
Lotilaner	Credelio (Elanco)	Dogs only	Both	1 month	X	No	Isoxazoline	2018
Lufenuron	Program (Novartis) and Sentinel (that also includes a heartworm pharma)	Both	Flea eggs, as well as hookworms, roundworms	1 month	No	X	Benzoylurea	1995 (for dogs)
Nitenpyram	Capstar (Novartis), Capguard (Sentry)	Both	Flea	A few hours only (meant for immediate infestation control)	X	No	Neonicotinoid	2000
Sarolaner	Simparica (Zoetis, a subsidiary of Pfizer)	Dogs only	Both	1 month	X	No	Isoxazoline	2016
Spinosad	Comfortis and Trifexis (Elanco)	Both	Flea	1 month	X	No	Spinosyn, macrocyclic lactone	2007 (approx.)

¹⁴ Flea products from the isoxazoline chemical family are new to the marketplace; therefore, pet health insights are largely limited to the studies conducted by the manufacturers and the packaging text required by the FDA. There appears to be no published information about health and safety beyond the manufacturer guidance in the MSDS. Due to the application method (pill), human exposure is likely small, though no data are available to verify this assumption.