March 24, 2020

Cody Kendrick
Office of Pesticide Programs (OPP)
Regulatory Public Docket Center (28221T)
U.S. Environmental Protection Agency (EPA)
1200 Pennsylvania Ave., NW
Washington, DC 20460–0001

Subject: Methoprene – Preliminary Registration Review Work Plan

Dear Mr. Kendrick:

On behalf of the Bay Area Clean Water Agencies (BACWA), we thank you for the opportunity to comment on the Preliminary Registration Review Work Plan for methoprene. Although not mentioned in the Federal Register notice, the preliminary workplan addresses two related compounds – kinoprene and hydroprene – which are also addressed in these comments. BACWA’s members include 55 publicly owned wastewater treatment facilities (“POTWs”) and 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, including several threatened and endangered species. 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 methoprene due to use in pet flea control products. The primary purpose of this letter is to request that the workplan be expanded to include an evaluation of sewer discharges from pet flea control products and other indoor methoprene, kinoprene, and hydroprene uses, such as at animal care facilities. Several studies, including a recent study involving several of our member agencies, suggest that pet flea control products have a direct pathway, via sewer collection systems, to municipal wastewater treatment plants.

BACWA appreciates that OPP has started to conduct evaluation of risks associated with pesticide discharges to the sewer system (“down the drain” risk assessments). OPP’s methoprene workplan
does not include a down-the-drain assessment. 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 US 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 Registration Review 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 pet flea control products and all other pesticide products with pathways to the sewer be carefully and thoroughly evaluated.

In addition to commenting on the preliminary workplan, we are also taking this opportunity to provide input on possible mitigation strategies for EPA to discuss with registrants. We are providing this input at this time because mitigation measures may be necessary and we understand based on the schedule in the work plan that the next opportunity for public comment may 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 treatment plants 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 treatment plants 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 Registration Review focusing on water quality impacts and for EPA to take action to ensure that any impacts are prevented or fully mitigated.

**BACWA requests that the work plan be expanded to include an evaluation of sewer discharges from pet flea control treatments and other indoor methoprene, kinoprene, and hydroprene uses**

BACWA is concerned that an evaluation of risks associated with indoor uses of these three chemicals was not included in the workplan and respectfully asks the EPA to include this analysis (a “down the drain” risk assessment) in the risk assessment. EPA has POTW predictive modeling tools that are suitable for conducting this assessment and has conducted similar assessments for many other pesticides.

We request that EPA specifically analyze sewer discharge sources such as:

- Pet spot-ons
- All other indoor treatments, such as at animal care facilities and any other facility that is likely to discharge to an indoor drain connected to a municipal sewer system

As explained in Appendix 1, pet flea control products contribute to POTW influent pesticides loads. Pet flea control chemicals are transported within a home to an indoor drain that flows to a POTW via the pathways illustrated in Figure 1.

**Figure 1. Methoprene Pathway: From Pet Treatments to Wastewater Discharge**

- **Indoor pet flea control product**
- **Washing of pets, hands, pet bedding, floors, carpets, and clothing**
- **Transport to sanitary sewer system**
- **Discharge to water body, recycled water, and/or biosolids**
Scientific studies detailed in Appendix 1 examined the pathways that transport active ingredients from pet flea control products 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 control products are significant sources of pesticides to POTWs that should be accounted for in the risk assessment.

Monitoring data for pet flea control chemicals in POTW influents and effluents show higher concentrations in northern California POTWs (Sadaria et al 2017). These data likely reflect real differences between these communities and those monitored in the nationwide study. The Sadaria et al. 2017 northern California study was conducted during a severe drought that triggered water use restrictions throughout the study area and significant reductions in POTW influent flows. Its September timing coincides with what may be the peak pet flea control season in the study area. According to Sadaria et al 2017:

“Higher overall concentrations and detection frequencies in effluent from northern California may reflect regional, seasonal, and/or climate-related differences from other sampled facilities, such as lower dilution caused by drought-related water use reductions, presence of pests during all seasons because of the mild coastal climate, and pesticide use responding to regional pest pressures (e.g., high flea populations in California coastal areas).”

BACWA requests that EPA methoprene modeling and mitigation approaches account for these factors. Please see Appendix 2 of BACWA’s comments on the Preliminary Ecological Risk Assessment for the Pyrethroid Insecticides (enclosed), where we detail potential approaches for addressing these factors within EPA’s current POTW model. BACWA has developed an approach for evaluating both acute and chronic toxicity of pet flea control treatments in the face of limited sales volume data, based on treatment frequency, per capita pet ownership, concentration of active ingredient, and estimated POTW removal efficiency (see BACWA’s Revised Appendix 4 of the Comments on the Preliminary Ecological Risk Assessment for the Pyrethroid Insecticides, October 20, 2017, attached).

“No Effects” determination under Endangered Species Act may need to be revisited

Since POTW discharges may contain methoprene, kinoprene, and hydroprene, OPP’s conclusion that there is “no exposure” to endangered aquatic organisms may not be correct. Endangered species may be exposed to these pesticides when POTW effluents flow into surface waters that contain endangered species. Consequently, OPP may need to revisit its “no effect” decision on Endangered Species Act Consultation.

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Information to support benefits assessment for pet flea control uses of methoprene

Because 100% of POTWs must comply with the Federal Clean Water Act 100% of the time, whenever EPA identifies significant risks to aquatic organisms from pesticides discharged to POTWs, BACWA believes that a robust exploration of risk mitigation is imperative. We provide the information below to support EPA’s benefits assessment for the pet flea treatment use of methoprene, in case EPA finds that methoprene discharges to the sewer pose a significant risk to aquatic organisms.

In response to the finding that pet flea control products are major sources of pesticides to POTWs, BACWA completed an assessment of pet flea control alternatives. This assessment, which is summarized in Appendix 2, identified multiple practical, effective, non-pesticide alternatives.

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

While we agree that pet flea and 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. Mechanical controls (vacuuming, washing of pet bedding) offer lower cost and greater long-term control, as these are the sole option that addresses all life cycle stages of fleas. Finally, we emphasize that we do not believe that fipronil, imidacloprid, indoxacarb, or pyrethroids are acceptable alternatives to methoprene.

Practical risk mitigation options exist

BACWA suggests that if significant risks to aquatic life are identified, EPA consider the following additional risk mitigation strategies for indoor methoprene products:

- **Determine the minimum application rate necessary to achieve pet flea control.** This would eliminate unnecessary overuse and minimize POTW discharge quantities. We understand that US EPA is in the process of completing new Guidelines for Efficacy Testing of Topically Applied Pesticides Used Against Certain Ectoparasitic Pests on Pets (docket EPA-HQ-OPP-2019-0161). When the new Guidelines are completed, methoprene pet treatments could be tested in accordance with multiple application quantities to determine the minimum necessary application quantity (by pet size).

- **Add schematic graphic to labels indicating that methoprene products like pet flea treatments should not be dumped down drains.** US EPA has proposed that pyrethroid insecticide products carry a graphic showing an image of an “X” or “⊗” over a drain on product packages. Methoprene, Kinoprene, and Hydroprene products should also carry these graphics. An example of such a schematic graphic is below (courtesy of Dublin San Ramon Services District).
• Require removal of any label language on pet spot-on products that encourages washing and water exposure of treated pets. Label statements such as “water proof” should be removed. All labels should dissuade owners from washing their pets for at least 2 weeks after treatment.

• Consider eliminating indoor aerosols products, which disperse chemicals in a way that significantly increases the likelihood that the active ingredient would be transported to the sanitary sewer, such as through mopping of floors. In contrast, containerized baits are unlikely to allow sewer discharges.

Thank you for the opportunity to provide this feedback regarding OPP’s Registration Review work plan for methoprene, kinoprene, and hydroprene. We ask that OPP evaluate methoprene, kinoprene, and hydroprene discharges to POTWs and the potential for subsequent POTW effluent toxicity, including to endangered species. If significant aquatic risks are identified, we request that OPP explore mitigation options, particularly for pet flea control products.

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

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Appendix 1

Pet Flea 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 flea control 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 sewage collection system and at POTWs.

Topical Pet Flea 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 flea control products. A study by California Department of Pesticide Regulation (CDPR) (Teerlink et al. 2017; enclosed) 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.”

Indirect Sewer Discharge Pathways
Several scientific studies have examined the transport of active ingredients from pet flea control 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.

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evaluated the transfer of permethrin and indoxacarb from a topical pet flea control treatment to people’s hands. 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 products onto human hands and through homes. 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 fluorescent dye into the spot treatment to provide photographic evidence of spot-on

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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.

- **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. 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. 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 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 topical flea control 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.

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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. 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 dinotefuran.

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. 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 flea control products may be the primary source of both chemicals in wastewater.

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9 See http://www.cdpr.ca.gov/docs/emon/surfwtr/presentations/presentation_130_targeted.pdf
Appendix 2

Pet Flea Control Products: Alternatives Analysis

Alternatives and Mitigation

BACWA requests that EPA, in coordination with CDPR (which has extensive relevant information and expertise), veterinarians, and registrants, develop mitigation strategies for pet flea control products, including spot-ons and collars. Two specific topics are discussed below, as an effort to provide insight regarding mitigation options for flea control:

- Alternatives: oral medications and integrated pest management appear effective
- Optimization of application rates of pet flea control products

Alternatives: Integrated Pest Management and Oral Medications

Mechanical controls (e.g., vacuuming) appear to be key to avoiding a flea infestation in a home. Further, since the previous registration, there is now an opportunity provided by oral treatments that have come on the market in recent years (available for both dogs and cats) that could avoid the on-pet use of not only dinotefuran, but also alternatives that are problematic from the water quality perspective (e.g., fipronil, pyrethroids, indoxacarb, and imidacloprid).

The fleas found on a pet are estimated to represent only 1-5% of the flea cycle in a home; the other 95% are found as eggs, larvae, pupae, and adult fleas throughout the home and surrounding environment. It takes about 18 days for a flea egg to grow into an adult flea, but in cool weather immature fleas can lay dormant in a pupal cocoon for up to 1 year. Adult fleas can live on a pet for 30 to 40 days. Fleas lay 20 to 50 eggs each day; consequently flea problems in residential settings can get out of control quickly.

Therefore, to avoid repeat infestations, one must address all stages of this flea cycle including flea eggs, larvae and pupae. One way to do so is via non-pesticide mechanical controls, including frequent indoor vacuuming, washing of pet bedding, and use of a pet flea comb. In particular, vacuuming needs to be both thorough and frequent. It should include the pet sleeping area, floors, furniture and all upholstered or carpeted surfaces, including under cushions, furniture and in other hard to reach places. Regarding frequency, it turns out that during the pupal stage, the flea is encased in a shell that is not penetrated by pesticides. The act of vacuuming can speed up the process. Specific guidance from one study notes the following:

"The vibration also stimulates adult fleas to emerge from their cocoons so that they can be collected in the vacuum machine. Therefore frequent vacuuming, during a flea infestation, can reduce the overall flea burden in the home. It should be ensured that vacuum bags are disposed of properly, to prevent recolonization of the home with flea stages previously removed by vacuuming."

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12 Ibid, 228-233. (enclosed)
14 "Biology, Treatment, and Control of Flea and Tick Infestations," Blagburn, B., and Dryden, M., Vet Clin Small
Although spot-on pet flea control products currently dominate the pet flea control market, new oral medications have recently become available. The table on the following page summarizes the current state of available oral medications for pets. The new pills, which are registered by U.S. FDA rather than EPA, appear to eliminate aquatic (and human) exposure pathways and should be equally or more convenient for pet owners, once they have obtained a prescription from a veterinarian. The involvement of the veterinarian has the added benefit of providing pet-specific guidance on flea control approach and safe dosage. Some studies indicate that oral medications may be more effective than topical spot treatments possibly because there is less reliance on proper application by the owner.\(^{15}\)

**Optimization of Application Rates of Pet Flea Control Products**

Another consideration for pet flea control products is that of application rate. Given that these household and pet flea control products have a transport pathway to the sewer, it would be of great interest to understand whether manufacturers have optimized the amounts applied. While spot-ons come in different doses based on pet weight, it is unclear whether that optimization was based solely on pet health or whether that is also the minimum dosage for effective insecticidal activity.

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\(^{15}\) “Flea blood feeding patterns in cats treated with oral nitenpyram and the topical insecticides imidacloprid, fipronil and selamectin,” McCoy, c., et al., Veterinary Parasitology, Vol. 156, pp 293-301, 2008.
### List of Currently Available Oral Pet Treatments for Fleas (Alphabetical)

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

16 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.