Chemicals in spot-on flea controls pollute water, studies show

UK and US research might lead veterinarians to rethink recommendations

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By Ross Kelly Po

Some scientists are urging veterinarians to weigh the potential environmental risks of spot-on flea treatments against their animal-health benefits, citing mounting evidence that the products' active ingredients are contaminating waterways.

Concerns about the ecological impact of certain flea controls have been stoked by new British research, which backs findings from recent studies in the United States but is contested by a study funded by spot-on manufacturer Elanco Animal Health.

Researchers involved in the British and supportive American studies are calling for tighter regulations that could include making prescriptions by a veterinarian mandatory or even banning the use of certain parasiticides.

The <u>British investigation</u>, funded by the United Kingdom government's Veterinary Medicines Directorate (VMD), identified high concentrations of the insecticidal chemicals fipronil and imidacloprid in thousands of samples taken from 20 English rivers.

The chemicals are active ingredients in many topical flea treatments, including in popular brands such as Advantage and Frontline Plus, that are applied to the skin of dogs and cats. The products long have been valued by the veterinary community for their effectiveness, ease of use and low toxicity in mammals, including humans. In addition to killing disease-causing fleas and ticks, however, their active ingredients also can kill tiny aquatic insects that are a crucial food source for fish and birds.

The toxicity extends to beneficial terrestrial insects, as well. Imidacloprid is a neonicotinoid, a class of pesticides implicated in harming bees. Fipronil, classified as a phenylpyrazole, is said to be <u>similar to neonicotinoids</u> in toxicity, physicochemical profiles and presence in the environment.



Photo by Clem Rutter via Wikimedia Commons

River Eden in Cumbria, England, was one of 20 English waterways from which samples showed high concentrations of fipronil and imidacloprid, active ingredients in common spot-on pet flea treatments. Some researchers hypothesize that the treatments contaminate waterways after being washed down drains when pets are bathed, owners clean their hands or pets swim in rivers. While work is underway to more definitively identify the pollution sources, the researchers believe flea treatments are likely a large contributor, partly because the use of fipronil and imidacloprid for agriculture is either restricted or otherwise uncommon in many places, including the U.K.

The magnitude of the problem is "very big," Dr. Martin Whitehead, a veterinarian at the Chipping Norton Veterinary Hospital in England and contributor to the British study, told the VIN News Service. "We regard this paper as an alarm call to the profession."

<u>Another study</u>, published in October and led by Colorado State University aquatic ecologist Janet Miller, found fipronil and related compounds were more toxic to stream communities than previous research had shown.

High levels of fipronil and imidacloprid also have been detected in eight San Francisco Bay water treatment plants, <u>according to research</u> published in 2016. A <u>separate study</u> in 2017, also conducted in California, found that spot-ons washed off pets as long as 28 days after they were applied. (The typical interval for reapplying topical flea control products is once a month.)

"We are consistently seeing both fipronil and imidacloprid concentrations in treated wastewater effluent that exceed chronic toxicity values for aquatic invertebrates, and that is of concern," Jennifer Teerlink, an environmental program manager at the California Department of Pesticide Regulation and a contributor to both California studies, told VIN News.

Teerlink added, and others concurred, that while flea treatments likely are a significant contamination culprit, further research measuring what proportion of chemicals are entering waterways from other possible sources, such as ant poisons, would be valuable information for regulators.

"They've got a smoking gun here, but the researchers haven't definitively shown where this contamination is coming from," Richard Wall, a zoologist and veterinary parasitology expert at the University of Bristol, said of the British research. "At the same time, when applying the precautionary principle, I think this issue has got to be taken really seriously."

'Novichock for insects'

The British analysis, led by Dr. Rosemary Perkins, a veterinarian and doctoral student at the University of Sussex, found fipronil and its even more poisonous derivative fipronil sulfone in virtually all of 3,861 samples collected by a U.K. government agency from 20 rivers between 2016 and 2018.

The mean concentration of fipronil and fipronil sulfone were 5.3 times and 38.1 times their chronic toxicity limits for aquatic invertebrates, respectively. Imidacloprid was found in 65.9% of the samples, with a mean concentration above chronic toxicity limits in seven of the 20 rivers.

Tellingly, samples taken closer to wastewater treatment plants showed higher concentrations of the toxicants, suggesting households were a large source of contamination, the authors said.

Furthermore, no agricultural use of fipronil has been recorded in the U.K. after 2015, and none of imidacloprid after 2016, with use in 2016 only minimal, according to the government Food and Environment Research Agency. Wall noted, though, that some farmers may have stockpiled chemicals and continued using them illegally, while Whitehead said some imidacloprid residue may have remained in the environment from previous use on crops.

The use of imidacloprid is still permitted on ornamental plants in the U.K., while imidacloprid and fipronil are found in ant and cockroach baits, though only one such product containing fipronil is licensed for use by people who aren't professional exterminators. "We don't have, in the U.K., much of a problem with ants and cockroaches on the whole, so the usage of those products is trivial on the scale of flea treatments," Whitehead said.

Dave Goulson, a University of Sussex biologist and expert on bees who also contributed to the British research, similarly has little doubt about the primary source of the water pollutants. "I really struggle to believe there's enough people buying ant poison for that to be a plausible explanation for the high level of contamination," Goulson said. "We know full well that we're dripping these chemicals onto our dogs and cats, so it seems to me that it's a no-brainer that that's where it's coming from."

The use of flea products in American and British households is common. In the U.K., for example, some 80% of the country's 9.9 million dogs and 82% of its 10.9 million cats are treated for fleas, according to the 2019 PDSA Animal Wellbeing Report. VMD data indicates that around 27.5 metric tons of fipronil and 33.0 metric tons of imidacloprid have been sold as flea treatments in the U.K. since their usage was approved in 1994 and 1997, respectively.

"If you had one teaspoon of one of these chemicals, that's enough to kill one-and-a-quarter-billion honey bees," Goulson said. "They're kind of the equivalent of Novichock for insects," he added, referring to a nerve agent widely suspected to be used by the Russian government to kill political dissidents.

Similarly, the San Francisco Bay study monitored concentrations from wastewater treatment plants. Researchers said the likely source of the toxicants detected was pet flea and tick products. "There is a high degree of certainty that spot-on treatments contribute a significant proportion of what we are seeing," Teerlink said.

Kelly Moran, a chemist and environmental consultant who also worked on that study, agrees. "We did a very detailed usage analysis, and fipronil, in particular, has very few allowed uses in California," Moran said.

Fipronil has never been licensed for agricultural use in California. Urban uses there include sprays for the outdoor perimeter of buildings to control ants and other insects, underground injections to control termites, gels for crack-and-crevice treatment and baits for insect control.

Regulators are concerned about the volume of pesticides that enter waterways from ant- and other insect-control products. In 2017, for instance, California introduced <u>new restrictions</u> on the application of lawn and premise sprays, including banning their use on garage doors and driveways during the months of November through February each year.

A spokesperson for Boehringer Ingelheim, which owns fipronil-based Frontline Plus, said the company is aware of the British and American studies and is "always evaluating and ensuring the safety" of its products. "Flea and tick products that contain fipronil must meet safety and quality requirements before they are approved by the authorities for commercial use," she said, offering the European Medicines Agency as an example of such an authority. Parasite-control developers are not required to assess the environmental risks of their products, however.

Sales of Frontline Plus in 2019 amounted to €379 million (US\$457 million), according to Boehringer Ingelheim. The patent on fipronil-based treatments, held by its developer Merial, expired in 2010, and now there are many generic products containing fipronil on the market. (Boehringer Ingelheim acquired Merial in 2017.)

A spokesperson for Elanco Animal Health, which owns imidacloprid-based Advantage, referred VIN News to the study that the company funded, published in November in the journal Environmental Sciences Europe.

In the peer-reviewed study, consultants hired by the company, working with staff scientists, developed a model for predicting water contamination levels for spot-ons, based on input parameters including historical sales-volume data and a survey of pet owners. The study concluded that using imidacloprid-based flea control products "does not pose a risk to aquatic wildlife if products are used according to the label and leaflet directions."

The Elanco spokesperson pointed to the benefits of the parasiticides: "It is important to underscore the critical role these products play in protecting the health and well-being of pets and their owners. Elanco flea and tick products prevent parasites, which can transmit serious diseases to both animals and people. They also play an important role in the fight against changing health threats and emerging diseases."

Elanco assumed ownership of Advantage last year when it acquired Bayer's animal health business. In 2019, sales of the Advantage family of products amounted to €418 million (US\$504 million), according to the latest publicly available financial data.

What should veterinarians do?

Whitehead, who also is co-director at Chipping Norton Veterinary Hospital, helped analyze data for the British research, tapping his previous experience in biomedical research. He said practitioners might want to advise clients to reduce their use of spot-ons. In cooler places especially, such as Britain, he said, there is little need for year-round application of topical solutions because fleas and ticks aren't as active during the winter. (Conditions vary widely depending on geography and climate.)

Whitehead noted that cutting back on sales could hurt veterinarians financially, or, if they work for corporate consolidators, risk the ire of managers wondering why they missed drug-sales targets. "We need to step back from that and think about whether we really need to be treating these animals so intensively all the time with these very powerful pesticides," he said.

Wall, the parasitology expert, cautioned that there are limits to how much pet owners can cut the use of flea control products before risking animal health. "Once an animal's got a flea infestation, it actually takes several months to get rid of it," Wall said. "So you do need to treat for reasonably long periods of time."

Flea infestations still can be a risk during winter, due to the use of household heating systems, Wall noted, although he agreed that the risk of tick-borne infections is much lower during the colder months.

He suggested that pollution risks might be reduced by prescribing orally administered flea treatments instead, which may be less likely to end up down the drain. "Fipronil and imidacloprid are quite old chemicals that are known to have a high level of toxicity to insects," Wall said. "There are lots of more modern chemicals to use that may have fewer environmental effects."

Popular oral treatment brands include Capstar and NexGard, which contain the chemicals nitenpyram and afoxolaner, respectively. Those chemicals are not without their own potential drawbacks. Nitenpyram, like imidacloprid, is a neonicotinoid. Afoxolaner is in a class of drugs known as isoxazolines that prompted an alert from the U.S. Food and Drug Administration in 2018 after being <u>associated with neurological problems</u>, including muscle tremors and seizures, in some pets.

Another possible disadvantage of oral products is that they may be harder to use, should pets, especially cats, balk at the idea of eating a tablet. Popular brands, however, are becoming more palatable by taking the form of

tasty chews or syrups that can be squirted into food or directly into pets' mouths.

If spot-ons must be chosen, sources recommend that pet owners avoid bathing animals soon after application. Still, Whitehead said the British researchers remain concerned that chemicals may wash off animals long after they've been treated.

"There are loads of ways in which these products can get into waterways," he added, noting that dogs, like people, are constantly shedding bits of dead skin and hair that can get washed down drains. "And all day long, dogs are lying on their bedding, and cats too, on cushions, or rubbing on your trousers and you're stroking them — things get washed and the chemicals can end up in the river."

Pesticides as a last resort?

For his part, the biologist Goulson would prefer veterinarians and pet owners apply the integrated pest management, or IPM, approach adopted by many in the farming sector. Essentially, it entails using pesticides as a last resort. Although orally applied treatments, Goulson said, pose a smaller risk than spot-ons, their active ingredients could still be excreted by pets and pollute the environment.

Whether IPM can provide adequate parasite control for animals that live indoors with people is an open question. Dr. Sharon Gwaltney-Brant, a veterinary toxicologist in the U.S., isn't convinced. "If your animal is outside, just keeping the parasite level down to where the animals aren't overtly stressed by them is a reasonable approach," she said. "But when you're bringing the animal into the household, where fleas and ticks pose a health risk to the people sharing furniture with their pets, that requires a much more intense approach than what IPM typically provides."

Many flea infestations occur while animals are outdoors, although Wall noted that transmission in the U.K. commonly occurs indoors, too. Most sources interviewed for this article concurred that regular vacuuming indoors, perhaps twice a week, can eradicate the eggs and larvae of fleas (which typically make up more than 90% of a flea infestation) and halt reproduction. Regularly laundering pet bedding can be helpful, too.

"It wouldn't be necessary to ban all use of fipronil and imidacloprid pet flea treatments to protect water quality," the U.S. chemist Moran said. "If we save them for where they're really necessary — like in emergencies when a whole household becomes severely infested — then society would maintain its ability to use these chemicals for a very long time."

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"Regular preventive treatment is important," but it's essential that products are used correctly, BVA junior vice president Justine Shotton said in an emailed statement. "Pet owners should speak to their vet for advice on the most suitable, risk-based treatment for their pet and its lifestyle, and about ways to reduce any environmental impact of the products they use."

On the regulatory front, the VMD confirmed to VIN News that the British study was part of wider research on pet flea treatments' environmental impact. The research is due to conclude in March 2023. "The VMD will consider its findings carefully, including whether any changes should be made to regulation of dog and cat flea and tick products in the light of the other available evidence," communications officer James Wood said.

In the U.S., Teerlink said the California Department of Pesticide Regulation is working to measure the relative contribution of different sources of fipronil and imidacloprid in waterways, including from outdoor residential use for purposes such as ant control. The department also has developed a permanent wastewater monitoring program, for which it has partnered with treatment plants across the state to get a better understanding of the pesticides' distribution.

Moran believes regulatory change in the U.S. and elsewhere is coming, in part because governments want to build projects that convert wastewater into drinking water. The conversion process, she explained, would create large volumes of toxic byproducts that would be difficult to dispose of, should use of chemicals like fipronil not be reduced.

"I think that vets are going to have an extremely important role in solving this problem," Moran said, "... so we're looking for their help."