



BEYOND PESTICIDES

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Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P),
Environmental Protection Agency,
1200 Pennsylvania Ave., NW.,
Washington, DC 20460-0001

Re: Pet Spot-On Analysis and Mitigation Plan; Docket No.: EPA-HQ-OPP-2010-0229

Dear Sir/Madam:

We are writing to provide comment on the agency's evaluation of pet spot-on products. In April 2009 the agency announced that it was intensifying its evaluation of spot-on pesticide products for flea and tick control due to a significant increase in the number of reported incidents. Incidents with flea and tick products involve the use of spot-on treatments, sprays, collars and shampoos. However, the majority of the incidents reported to the agency are related to flea and tick treatments with EPA-registered spot-on products. Spot-on products are generally sold in tubes or vials, and are applied to one or more localized areas on the body of the pet, such as in between the shoulders or in a stripe along the back. The agency is now taking a series of actions aimed at increasing the safety of spot-on pesticide products for flea and tick control for cats and dogs, and will begin reviewing labels to determine which ones will require new instructions and labeling for spot-on flea products.

The agency is recommending restrictions and amendments to products to include: (1) dosing, (2) distinguishing between cat and dog products (3) improving label clarity, and (4) addressing uncertainties about 'inert ingredients.' The agency is also proposing to tighten regulations regarding pet products by improving data requirements, standardizing reporting, as well as granting conditional registration for new products. While the agency's recommendations are worthwhile and necessary to make label language more user-friendly to provide more information to consumers, the agency has missed the underlying problem that will continue to plague this sector of consumer products; hazardous pet product ingredients.

Historical Perspective

Addressing problems associated with pet products and high adverse incidents are not new for the agency. In 1988, Hartz Mountain Corporation was forced to remove its flea and tick product, Blockade, after reports of 200 pet deaths and charges filed by EPA for the company's

failure to report adverse effects incidents. In 2000, EPA again received mounting reports of adverse effects to pets, especially cats, which prompted the agency to investigate the incidents. After an investigation, similar to the one recently conducted, EPA proposed label amendments for the products sold by Hartz Mountain Corporation. Label changes included changing the “stripe-on application” method to specify a “spot-on” application. By 2002, an agreement was reached with Hartz to cease sale and distribution of, and implement a product recovery, label improvement and consumer education program for its products, as well as recover, repackage and re-label available stock.¹ The agency intended with these actions to include stronger precautionary statements and use directions for the relabeled products, and to initiate with the registrant a call for new submissions of additional animal safety studies conducted by an independent laboratory and submissions of additional quarterly reports specific to cats, summarizing allegations of toxic or adverse incidents. By 2005, EPA insisted that Hartz Mountain Corporation cancel uses of several flea and tick products that may be associated with a range of adverse reactions, including hair loss, salivation, tremors and numerous deaths in cats and kittens. Once again the agency called for relabeling which included animal weight and age specifications.²

However, adverse incidents among treated pets keep mounting in spite of previous relabeling efforts. According to the agency, incidents rose by 53 percent between 2007 and 2008. What is not clear is why the agency continues to focus on mitigation through constant relabeling efforts. Relabeling has not decreased the incidents of pet poisonings and consumer error cannot alone be held responsible for the sharp increase in incidents. The agency must therefore reevaluate its assessment methods and broaden its scope, in order to effectively address the issue. This would include taking a closer look at *all* product ingredients and removing from products those which, as a result of their toxicity, pose unreasonable risks to pets and humans alike.

The Real Problem Is Not The Product Label But Product Ingredients

According to the agency’s evaluation, many of the pet products reviewed and associated with adverse incidents contain the following active ingredients: amitraz, cyphenothrin, dinotefuran, etofenprox, fipronil, imidacloprid, permethrin, phenothrin, pyriproxyfen, and s-methoprene, under brand names such as Frontline, Sergeant, Hartz and Advantage. Pyrethroids such as cyphenothrin, permethrin, phenothrin are neurotoxicants that affect the central nervous systems of mammals. Clinical signs in small animals during a pyrethroid toxicosis vary but are

¹ USEPA. 2002. Label Instructions Tightened on Flea & Tick Control Products for Pets. EPA News Release: available at <http://yosemite1.epa.gov/opa/admpress.nsf/6427a6b7538955c585257359003f0230/3314cec47831c91885256c7e005e618a!OpenDocument&Start=4.1&Count=5&Expand=4.4>

² USEPA, 2005. Hartz to Relabel and Cancel Flea and Tick Drops for Cats and Kittens. EPA News Release: available at <http://yosemite.epa.gov/opa/admpress.nsf/be9354c9b783ef00852572a00065593f/5c939b447d62b1f385257015007c6765!OpenDocument>

generally attributable to neural dysfunction.³ In laboratory rats, pyrethroids caused a syndrome consisting of aggressive sparring, increased sensitivity to external stimuli, and fine tremors progressing to whole-body tremor and prostration.⁴⁵ In general, cats are highly sensitive to permethrin and inappropriate or accidental application of these products could be fatal. Though they are mostly used on dogs, even small amounts of permethrin spot-on products can cause severe clinical signs in cats.⁶ Members of this class of chemicals are also possible carcinogens (permethrin), endocrine disruptors (cyphenothrin, permethrin) and may cause reproductive effects (permethrin).⁷

Neonicotinoids (imidacloprid, dinotefuran), a relatively new class of pesticides, are also associated with organ damage, and neurotoxic effects. Dinotefuran, a broad spectrum insecticide, causes decreased motor activity seen after acute dosing and increased motor activity after repeated dosing.⁸ It may also be responsible for endocrine-related toxicity manifested in the reproductive toxicity studies (in rats) as decreases in primordial follicles and altered cyclicity in females, abnormal sperm parameters in males. Changes in testes and ovary weight were also seen in several species, including dogs.⁹ Similarly, imidacloprid is linked to reproductive and mutagenic effects, - it has been determined that imidacloprid increased the frequency of genetic damage by chemically binding to DNA - as well as neurotoxic effects as manifested by tremors, uncoordinated gait and decreased activity.¹⁰

Amitraz seems to be the most toxic when it comes to pets. It is moderately toxic and is associated with liver toxicity. Studies with beagle dogs resulted in liver, kidney, and central nervous system effects. Chronic toxicity studies using dogs resulted in central nervous system depression, increased blood glucose levels, and hypothermia. The agency has classified it as a Group C (possible human) carcinogen based on lymphoreticular tumors, liver and lung tumors produced in female mice. Amitraz also exhibited developmental and neurotoxic effects in other studies.¹¹ The other ingredients, such as fipronil, are all associated with some degree of neurotoxic and/or endocrine disrupting effects. Fipronil in particular is an endocrine disruptor,

³ Valentine WM, 1990. Toxicology of selected pesticides, drugs, and chemicals. Pyrethrin and pyrethroid insecticides. *Vet Clin North Am Small Anim Pract* ;20(2):375-82.

⁴ Cantalamessa, F. 1993. Acute toxicity of two pyrethroids, permethrin, and cypermethrin in neonatal and adult rats. *Arch Toxicol* (1993) 67:510-513 Archives of

⁵ Sutton, N.M. et al. 2007. Clinical effects and outcome of feline permethrin spot-on poisonings reported to the Veterinary Poisons. *J. Feline Med & Surgery*,9(4): 335-339

⁶ Richardson, J. 2000. Permethrin Spot-On Toxicoses In Cats. *The Journal of Veterinary Emergency and Critical Care*

⁷ Beyond Pesticides' Factsheets available at

⁸ USEPA. 2004. Dinotefuran Pesticide Fact Sheet. Office of Prevention, Pesticides and Toxic Substances. Washington DC

⁹ Ref #8

¹⁰ INCHEM. 2001. Toxicological Evaluations: Imidacloprid. International Program on Chemical Safety(IPCS) <http://www.inchem.org/documents/jmpr/jmpmono/2001pr07.htm#2.2.3>

¹¹ USEPA. 1996. Amitraz RED Facts. Office of Prevention, Pesticides and Toxic Substances. Washington DC

disrupting thyroid function,¹² and a group C (possible human) carcinogen.

The agency must reconsider the use of these hazardous chemicals in pet products to which dogs, cats and humans are vulnerable. Cats and dogs are vulnerable to long-term exposures to these chemicals. Their smaller body size makes them more susceptible to chemicals which they absorb through mucous membranes of mouth, nose, and eyes into bloodstream and through skin, liquids and powders that stick to their fur. Cats can absorb more chemicals than dogs due to their unique grooming habits, while dogs respond to many toxic insults in ways analogous to humans. Cancer is one of the leading causes of death in dogs and cats today.¹³ Compared to humans, dogs develop tumors twice as frequently. Glickman et al. found a significant increase in the risk for bladder cancer by topical insecticide use (which was enhanced in overweight or obese dog).¹⁴ A 2003 study by Bertone et al. found that cats that wear flea collars have five times the risk of oral squamous cell carcinoma (a form of skin cancer) than those that do not wear flea collars.¹⁵

Humans are also at risk for long term exposures. A 2009 U.S. Geological Survey (USGS) study found that residences with a pet on which a flea-control product containing fipronil was used were among homes with elevated fipronil concentrations, and concentrations 15 times higher indoors than those found outdoors.¹⁶ Children and adults alike, while playing and stroking pets, will come into contact with these chemicals which lead to dermal exposures. Human oral exposures can also occur through hand-to-mouth transfer after petting treated animals.¹⁷ One study detected residues on gloves worn while petting treated dogs for 5 minutes, with high concentrations detected up to 24 hours after application.¹⁸ Human exposures to these toxic pesticides can give rise to acute and chronic symptoms mentioned above.

Inert Ingredients in Pet Products

EPA is to determine whether additional information on certain 'inerts' is needed and, if so, would seek to obtain that information. The agency also proposes that when 'inerts' with suspected toxic effects are identified, EPA will not allow the use of these chemicals in pet products. Beyond Pesticides has long been advocating for the disclosure and removal of

¹² Leghait J, Gayraud V, Picard-Hagen N, Camp M, Perdu E, Toutain PL, Viguié C. 2009. Fipronil-induced disruption of thyroid function in rats is mediated by increased total and free thyroxine clearances concomitantly to increased activity of hepatic enzymes. *Toxicology* 255(1-2):38-44.

¹³ Rusk, Anthony. 2005. Cancer: Cases likely will rise in aging animals. *DVM Newsmagazine*, Mar 1.

¹⁴ Glickman, L. et al. 1989. Epidemiologic study of insecticide exposures, obesity, and risk of bladder cancer in household dogs. *J. Tox. Environ. Health*; 28(4), 407 – 414.

¹⁵ Bertone ER., LA. Snyder, AS. Moore. 2003. Environmental and lifestyle risk factors for oral squamous cell carcinoma in domestic cats. *Journal of Veterinary Internal Medicine* 17(4): 557–562.

¹⁶ Mahler, B et al. 2009. Fipronil and its Degradates in Indoor and Outdoor Dust. *Environ. Sci. Technol.*, 43 (15):5665–5670

¹⁷ CDPR. 2009. Fipronil [CASRN: 120068-37-3] Materials for the July 28-29, 2009 Meeting of the California Environmental Contaminant Biomonitoring Program (CECBP) Scientific Guidance Panel (SGP). California Department of Pesticide Regulation

¹⁸ Jennings KA, Canerdy TD, Keller RJ, Atieh BH, Doss RB, Gupta RC. 2002. Human exposure to fipronil from dogs treated with frontline. *Vet Hum.Toxicol.* 44(5):301-3.

hazardous inert ingredients from all consumer products (*Please see Beyond Pesticides Comments regarding Disclosure of Inert Ingredients docket number EPA-HQ-OPP-2009-0635*). In doing so, the agency ensures that consumers have the information they need to make well-informed decisions surrounding the products they purchase that are beneficial of their health and that of the environment. EPA must move quickly to remove hazardous ingredients from consumer products and disclose all inert ingredients.

Advocate for Safer Alternatives

Many alternatives are available to consumers who do not wish to poison themselves or their pets. Simple routines such as frequent grooming and bathing, regular vacuuming, steam cleaning and laundering to control fleas and ticks are effective at keeping fleas and ticks at bay. Special combs are available that help remove adult fleas from the coat of a shorthaired pet. If there is a need for chemical control, herbal or natural products that contain cedarwood, lemongrass, peppermint, rosemary and thyme can be used to treat pets. The agency must encourage registrants to seek out new, least toxic ingredients that can be used safely on pets.

Conclusion

The agency must realize that its traditional approach to regulation based on the product label does not go far enough to protect pets or their human companions. Instead of repeating past, ineffective regulatory action that would inevitably lead to more adverse incidents, the agency must move to restrict the use of these hazardous chemicals in these pet products.

Thank you for your consideration.

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