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February 16, 2010

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

RE: Registration Review; Pesticide Dockets Opened for Review and Comment (Cyphenothrin)
(Docket ID EPA-HQ-OPP-2009-0842-0001)

Dear Sir or Madam:

Thank you for the opportunity to comment on the registration review of the pesticide cyphenothrin. BioSpotVictims, a non-profit organization which seeks to educate the public on the potential hazards of pet pesticide products, would like to express serious concerns over the continued registration of cyphenothrin-based flea and tick products for pets.

In November 2006, EPA granted conditional approval to three cyphenothrin-based pet products for dogs, which were registered to Sergeant's Pet Care Products, Inc. Each of these products contains a high concentration (40%) of cyphenothrin – a Type II pyrethroid insecticide. **No other registered spot-on product for flea and tick control contains a Type II pyrethroid.**

According to Synthetic Pyrethroids and Paresthesia (a NPIC Fact Sheet) there is evidence that synthetic pyrethroids containing an alpha-cyano group (such as cyphenothrin) are more potent in eliciting neurotoxic effects, in comparison to pyrethroids that do not contain an alpha-cyano group (such as permethrin).

The acute neurotoxicity of pyrethroids has been well characterized, and animal studies suggest the potential for developmental neurotoxicity. Acute exposure to pyrethroids has been shown to result in skin irritation, dizziness, and tremors. It can aggravate asthma or lead to asthma-like symptoms.

In June 2005, prior to registration of Sergeant's cyphenothrin-based products, EPA raised concerns over "significant inconsistencies" between the results of the companion animal safety study and the efficacy study for these products. Here is the memorandum:

<http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/129013/129013-2005-06-27a.pdf>

Excerpt:

"The occurrence of neurological signs of toxicity in all 6 dogs in the efficacy study suggests that there is not even a 2X margin of safety associated with the proposed application rate of 1.17 mL in at least some dogs weighing from 6.8 - 15 kg, while the efficacy study data, as submitted, were conducted using a dose rate higher than that of the previously reviewed proposed label."

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In July 2005, Sergeants informed the EPA that the dose rate used in the efficacy study was in fact the 1X application rate, and that the effects observed in the study (vomiting, head shaking, pacing, and tremors) could be considered to be “normal dog behavior.”

However, EPA concluded that the “most likely explanation for the symptoms (including tremors) observed in the efficacy study was that the dogs ingested some of the test material after application.” EPA proposed a label revision to the application instructions to prevent dogs from ingesting it. Here is the memorandum:

<http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/129013/129013-2005-10-12a.pdf>

Excerpt:

“Current directions for the application of this product specify to apply as a stripe from the back of the neck to base of the tail. If labeling is revised to specify application of the product from the back of the neck to a point midway between the neck and tail then the dog would not be able to reach any part of the application site and so would be unable to ingest the product by licking. With this revision, TRB would have no objections to the registration of the proposed product.” **No other registered spot-on product instructs pet owners to apply it in that manner.**

The companion animal safety study for Sergeant’s cyphenothrin-based products should be classified as **unacceptable** because the amount of test material applied to each dog was **significantly lower** in volume than the application rates that are currently registered. For example, dogs weighing 15-33 lbs. received a 1.5 mL dose, not the 3.0 mL dose that is currently registered for dogs weighing 21-39 lbs.

Here is the companion animal safety study:

<http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/129013/129013-2004-11-24b.pdf>

Due to the significantly lower doses that were used in the companion animal safety study, it has not been established that there is an adequate margin of safety (at least 5X) between the exposure associated with the labeled use level for this formulation in dogs and that at which significant adverse effects may occur.

In addition, EPA did not require a new companion animal safety study to determine if the proposed revision to the application instructions effectively mitigated the adverse effects, nor did it require the registrant to disclose on the label the potential for harmful effects if ingested by dogs.

In March 2006, EPA found additional concerns about Sergeant’s cyphenothrin-based pet products. An occupational and residential exposure assessment determined that toddler residential risk estimates for pet contact and hand-to-mouth activity were both risks of concern. Here is the memorandum:

<http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/129013/129013-2006-03-20a.pdf>

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Several of EPA's assumptions that were used in the above residential exposure assessment were deeply flawed. It assumed that a 5% application rate was initially available to transfer from pet to human (not the 20% standard value from HED's residential exposure SOPs). Its calculations were based on a 3 year old toddler, expected to weigh 15kg (representing an average weight from years one to six), despite the fact that children under the age of two weigh considerably less and exhibit hand-to-mouth activity at a much higher frequency than a 3 year old. It also based its calculations on a dog weighing 30 lbs. (chosen as a representative animal), and assumed an even loading of residue across the entire surface of the dog on the day of application, despite the fact that larger dogs require significantly larger application rates, and an even loading of residue across the entire surface of the dog takes more than 24 hours to occur (making recently treated pets even more of a danger for toddlers).

However, the most disturbing aspect of the above residential exposure assessment is the fact that an incorrect application rate was used in the calculation. Instead of using 1200 mg ai/treatment for dogs 21-39 lbs., EPA used 645 mg ai/treatment for dogs 15-33 lbs. If the correct application rate had been used, the risks of concern would have been even more alarming. The application rate that ought to be used is the maximum dose specified on the label, which happens to be 2400 mg ai/treatment for dogs over 61 lbs. because that represents the worst case scenario for toddlers on the day of application.

Last June, EPA consulted the OPP Incident Data System for poisoning incident data on cyphenothrin. Here is the memorandum:

<http://www.biospotvictims.org/EPA-HQ-OPP-2009-0842-0003.pdf>

The purpose of the database search was "to identify potential patterns on the extent and severity of the health effects attributed to cyphenothrin exposure." The search found 27 incidents occurring in the United States from 2002 to the present – **all but one involved Sergeant's pet products.**

Despite the fact that the reported symptoms (included skin irritation/pain, ocular irritation/pain, dizziness, and shortness of breath) were consistent with the acute effects of pyrethroid exposure, and all but one of the incidents involved Sergeant's pet products, the Health Effects Division of EPA concluded the following:

"The evaluation of incident data for cyphenothrin chemicals has reported (relatively low volume of incident, no moderate or severe health effects that are plausibly related to the pesticide in question, based on toxicological data, sporadic incidents of an undefined or non-specific nature such as that clear trends or patterns cannot be discerned) only 27 number of incidents, symptoms appear generic and not confirmed to be related to exposure, there is no clear evidence of a trend or exposure pattern. Therefore, at this time, there are no remarkable case reports which suggest a plausible association between a moderate or severe health outcome and exposure to pesticide cyphenothrin nor can we discern any suggestion of a trend or pattern regarding the health effects due to the alleged exposure to pesticide cyphenothrin. The current review of the incident data does not warrant further investigations at this time."

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EPA did not search any other database for poisoning incident data on cyphenothrin, and stated that it “is supplying the following incident report to fulfill our requirement to docket summaries of incident data that were reported to the Agency.”

Last August, EPA prepared a human health assessment scoping document in support of the registration review of cyphenothrin. Here is the memorandum:

<http://www.biospotvictims.org/EPA-HQ-OPP-2009-0842-0002.pdf>

Here are excerpts:

“Signs of pyrethroid neurotoxicity typically include tremors and convulsions, and death at sufficiently high doses. This mechanism of action is shared by both insects and mammals.”

“The target organ for cyphenothrin is the nervous system, with neurotoxic effects observed in toxicity studies in rats, mice, and dogs. Effects observed include: tremors, convulsions, piloerection, salivation, decreased activity, and irregular respiration. Additionally, liver toxicity was seen in rats and mortality was observed in rats, mice, and dogs at high doses. No adequate dermal or developmental toxicity studies are available for cyphenothrin...”

“In accordance with the revised 40 CFR Part 158 guidelines, the toxicological database is incomplete at this time, and the following additional toxicology data are required to support registration review:”

- 870.3250 90 Day Dermal Toxicity Study in Rats
- 870.3700 Developmental Toxicity Study in rats
- 870.3700 Developmental Toxicity Study in Rabbits
- 870.6200 Acute Neurotoxicity Study
- 870.6200 Subchronic Neurotoxicity Study
- 870.6300 Developmental Neurotoxicity Study (cite previously submitted DNTs as alternative)
- 870.7800 Immunotoxicity Study

“During registration review, a quantitative residential exposure assessment must be performed to address potential risk associated with cyphenothrin uses on treated pets, aerosol sprays and total release aerosols or foggers for the control of insects in indoor/outdoor residential settings. HED/OPP is currently revising the Residential Standard Operating Procedures (SOPs), including those used to determine exposure associated with treated pets and uses in indoor settings. Reviewers should incorporate new guidance from the Treated Pets and Indoor SOPs to refine exposure estimates associated with residential handler and postapplication exposure (including hand-to-mouth) resulting from use of cyphenothrin.”

“Dermal toxicity and dermal penetration studies are not available for cyphenothrin.”

“The toxicology database for cyphenothrin is not complete.”

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“Combined MOEs estimated for exposures to children from hugging treated companion dogs are of concern. However, the MOEs were calculated using an endpoint from a subchronic study (90-day dog) and companion exposures to treated pets were assessed on a day 0 (i.e., on the day of application) exposure. As a result, the MOEs were not of concern when the characterization of the selection of the endpoint and dose for risk assessment were considered. As part of the registration process for the spot-on products, a petting/stroke study was required as a condition of registration. Although a protocol for this study was submitted, the Agency concluded the study involved intentional dosing with a pesticide. Pending evaluation of the revised Residential SOPs, and the identification of additional data needs for evaluation exposure associated with pesticides used on pets, no further action has been taken to develop chemical-specific data for cyphenothrin. Therefore, the lack of the data remains a deficiency.”

“There do not appear to be any particular socioeconomic subgroups that may experience a higher degree of exposure to cyphenothrin.”

Last April, EPA issued an advisory due to a sharp increase in the number of incidents (including pet deaths) reported from the use of spot-on flea and tick products. In 2008, over 44,000 adverse incidents were reported to the EPA – many of which involved Sergeant’s cyphenothrin-based pet products.

An analysis of EPA adverse incident data from July 1, 2006 - June 30, 2008 revealed that Sergeant’s cyphenothrin-based products accounted for **43% of all adverse incidents involving spot-on products, and 67% of adverse incidents involving pyrethroid-based spot-on products.** Here is the analysis:

<http://www.biospotvictims.org/AdverseEventsData.pdf>

EPA should view these incidents as an environmental justice issue. Pet owners who cannot afford to purchase safer flea control products from their veterinarian also cannot afford the cost of veterinary care when their pet experiences an adverse reaction to an inexpensive over-the-counter product.

For all of the reasons stated above, it is clear that Sergeant’s cyphenothrin-based products pose unreasonable and unacceptable risks to children and pets.

BioSpotVictims urges EPA to adhere to its mandate to protect the public from unreasonable risk by canceling the registration of Sergeant’s cyphenothrin-based products, effective immediately.

Sincerely,

James TerBush
Website Administrator