CONFIDENTIAL BUSINESS INFORMATION

October 28, 1998

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MEMORANDUM

SUBJECT: Review of Domestic Animal Incident Data for Tetrachlorvinphos

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EXECUTIVE SUMMARY

Tetrachlorvinphos is registered for direct application to multiple animal species. The domestic animal incident reports for 1997 were reviewed. The vast majority of the incidents were from Hartz Mountain Company, which has a toll-free number on its product labels. Calls are evaluated by the American Society for the Prevention of Cruelty to Animals/Animal Poison Control Center (ASPCA/NAPCC), which classifies causality into the following categories: doubtful, low, moderate and high suspicion. For cats, there were a total of 33 calls for products containing 1.07-1.08% tetrachlorvinphos; 3 (including one death) were classified as high suspicion, 12 as moderate suspicion, 12 as low suspicion and 6 as doubtful. There were a total of 12 calls for products containing 2.8-3.0% tetrachlorvinphos; 2 were classified as high suspicion, 4 as moderate suspicion, 1 as low suspicion and 5 as doubtful. There were a total of 14 calls for products containing 14.55% tetrachlorvinphos; 6 were classified as low suspicion and 8 as doubtful suspicion. For dogs, there were a total of 6 calls for products containing 1.07-1.08% tetrachlorvinphos; three were classified as low suspicion and three as doubtful suspicion. There were a total of five calls for products containing 14.55% tetrachlorvinphos; 1 was classified as

low suspicion and 4 as doubtful. The clinical signs seen in those cases classified as moderate and high suspicion were typical of organophosphate poisoning (ataxia, salivation, vomiting, diarrhea and tremors).

There were an additional five incidents in the Incident Data System involving cats, dogs and cattle. One kitten died, however, it was treated excessively with a 1.07% product.

Only limited conclusions can be drawn about the incident data due to the following: 1) the actual number and type of incidents reported to Hartz Mountain cannot be determined due to confusing data submissions; and 2) no incidence rates can be determined because there are no data on the amount of product sold or applied. The conclusions which can be made are: 1) cats are more likely to be involved in incidents of adverse reactions with tetrachlorvinphos[1]; 2) the lower concentrations of tetrachlorvinphos are more frequently associated with adverse reactions that have a high degree of causality. The product involved in most of the incidents was Hartz 2 in 1 Flea & Tick Pump for Cats II (Reg. No. 2596-126), which contains 1.08% tetrachlorvinphos as a single active ingredient. It is recommended that Companion Animal Safety Studies are conducted on those products which were registered prior to this requirement.

REVIEW

Tetrachlorvinphos Products Registered for Veterinary Use

Tetrachlorvinphos is registered for use in the control of fleas and ticks on dogs and cats in multiple concentrations, formulation types (powders, sprays, collars, etc.) and as single or active ingredient products. There are also registered uses on horses, cattle and poultry, mostly for fly control. **The number of products registered with Domestic Animal Safety Study data is unknown.**

Incident Data Review

The vast majority of the adverse reaction incidents submitted to EPA are from the Hartz Mountain Company, the registrant of most of the products for use on dogs and cats. Hartz Mountain provides a toll-free number on its products. If calls concerning a sick animal are received by the company, they are referred to the American Society for the Prevention of Cruelty to Animals/Animal Poison Control Center (ASPCA/NAPCC), a poison control hotline for animals. This hotline not only offers advice on treatment to animal owners and veterinarians but also investigates incidents and classifies them according to the likelihood that the product was responsible for clinical effects. Classification categories include doubtful, low, moderate and

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[1] In gen complications submitted eral, cats are more sensitive to pesticides because, as compared to other domestic animals, they are relatively deficient in their ability to conjugate xenobiotics with glucuronic acid which is the most important step in the metabolism of such substances.

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high suspicion. Hartz Mountain claims that the incident reports submitted to EPA are **CONFIDENTIAL BUSINESS INFORMATION**. Therefore, they are not entered into the Incident Data System (IDS) but are forwarded to the Product Manager and to the science divisions for review and evaluation. The incidents are submitted as quarterly reports for all of the Hartz products. Separating out and summarizing the incidents for an individual chemical is very labor-intensive. Therefore, only the data submitted for the calendar year 1997 were reviewed. It is assumed that this year is representative of the findings for other years.
The following table summarizes the Hartz Mountain incidents by species, percentage of active ingredient and ASPCA/NAPCC classification for 1997.

	Cats			Dogs		
	1.07-1.08%	2.8-3.0%	14.55%	1.07-1.08%	2.8-3.0%	14.55%
Doubtful	6	5	8	3	-	4
Low	12	1	6	3	-	1
Moderate	12	4	-	-	-	-
High	3*	2	-	-	-	-
Total	33	12	14	6	-	5

* Includes one death.

There was also one ferret which was treated with a 1.08% formulation that was classified as doubtful. The clinical signs seen in those cases classified as moderate and high suspicion were typical of organophosphate poisoning (ataxia, salivation, vomiting, diarrhea and tremors). The product responsible for most of the incidents in cats was Hartz 2 in 1 Flea & Tick Pump for Cats II (Reg. No. 2596-126), which contains 1.08% tetrachlorvinphos as a single active ingredient.

Hartz Mountain also submits a summary of adverse incident reports received directly by the company. This summary only lists registration number and the number of calls. The amount of overlap of reports in this summary and in the ASPCA/NAPCC data is unknown. The cover letter with the quarterly reports from Hartz Mountain only states that "some of the reports in this summary may be duplicated in the NAPCC compilation". The number reported for 1997 by percentage active ingredient is as follows:

1.07 - 1.08% - 39
2.8 - 3.0 - 4
14.555% - 35

There were five new incident reports in IDS for 1997. One involved a 4 month-old dog that developed nervous system signs typical of organophosphate poisoning 3-4 hours after a 14.55%

tetrachlorvinphos collar was applied. The animal recovered with treatment. The veterinarian stated that he had a high suspicion that the collar was responsible for the signs. The second report involved a 5 year-old Doberman dog that became anaphylactic after being treated with a 3.0% tetrachlorvinphos powder registered for use on cats. In the third case, a 6-8 week-old kitten died after receiving multiple treatments with a 1.07 % spray over a two-week period. In the fourth case, a two year-old cat developed excessive salivation and tremors after application of a 1.08% tetrachlorvinphos spray; the animal recovered with treatment. In the fifth report, a farmer mixed diesel fuel with Ravap E.C. Livestock, Poultry and Premise Insecticide (23% tetrachlorvinphos and 5.7% dichlorvos) and applied it to the backs of 30-50 head of cattle. Two days later, the animals displayed abnormal behavior, including running through fences. They were also observed to have their tongues hanging out, were breathing hard and salivating. They recovered after the product was washed off. Except for the first case, there was no evaluation of causality.

Veterinary Literature

There is very little information about poisoning incidents with tetrachlorvinphos in the veterinary literature. The NAPCC (before joining with ASPCA) has published several yearly incidences of poisonings in domestic animals. In the 1984 report, the incidences of individual agents were not reported, however insecticides ranked number one and two in exposures for cats and dogs, respectively. It was noted in the article that although tetrachlorvinphos is of very low toxicity in most species, cats may be somewhat predisposed to toxicosis from this agent.[2] In 1986, a list of the top generics with causality classifications for poisonings was published.[3] Tetrachlorvinphos was not on the list of the top generics (human and animal drugs, plants, household products, etc.) for either dogs or cats. However, the article does state that from 1986 through 1987 there were a total of 35 calls pertaining to dogs and cats. The article goes on to say that although this compound is much less toxic than most other organophosphate insecticides, there were calls that were assessed as toxicosis or suspected toxicosis (the two highest causality classifications at that time). These were primarily the result of exposure of cats to flea spray and powder formulations.

A list of the top 25 generic agents involved in calls to NAPCC in 1992 was published, but the nature of the call, incidence rates and causality were not provided.[3] Tetrachlorvinphos was number 11 on the list for cats; it was not on the list for dogs.

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[2]Beasley VR. Prevalence of Poisonings in Small Animals. In: Kirk RW (ed.) Current Veterinary Therapy IX. Philadelphia: W.B. Saunders Co., 1986, pp. 120-129.

[3] Beasley VR, Trammel HL. Incidence of Poisonings in Small Animals. In Kirk RW (ed.) Current Veterinary Therapy X. Philadelphia: W.B. Saunders, 1989, pp. 97-113.

[3] Buck WB. Top 25 Generics Involving Dogs and Cats Managed by the National Animal Poison Control Center in 1992. In Bonagura JD (ed.) Kirk's Current Veterinary Therapy XII. Philadelphia: W.B.Saunders Co., 1995, p. 210.