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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 29 1984

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Precautionary Labeling for Hartz Rabon Dog Collar

TO: George LaRocca (PM 15)
Registration Division (TS-767)

FROM: Byron T. Backus
Toxicology Branch
HED (TS-769)

THROUGH: Robert Zendzian, Ph.D., Acting Head
Review Section III
and
William Burnam, Chief
Toxicology Branch

Product: Rabon Dog Collar

Registration: 2596-62

Tox. Chem. 217A

Registrant: Hartz Mountain Corp.

Action:

This is a request for a review of a registrant response to a previous Toxicology Branch review of 3/13/84. Part of the response is a final report titled Effects of the Use of An SD-8447 Collar on Puppies.

Conclusions:

The material received 7-13-84 does not adequately address the questions raised in the toxicology review of March 13, 1984. In particular, there is no response to the possibility (suggested by one study) that pups may have reduced weight gains as a result of exposure during their first four weeks of life to a collar worn by the bitch.

The study titled Effects of the Use of An SD-8447 Collar on Puppies has been classified as invalid. Some of the deficiencies in this study include lack of identification of the active ingredient (and its percentage) in the SD-8447 collar, and lack of data (sexes, which were sick and medicated with Chloramphenicol, total

number of puppies in each litter) regarding the individual animals. Also, there were no RBC or plasma cholinesterase activity measurements, which would be considered appropriate for even such a weak cholinesterase inhibitor as Rabon (assuming this was the active). However, even with these data the study could not be considered relevant to the question of toxicity to newborn puppies as the animals were already 4 weeks old when the collars were placed on them.

Finally, even in this study there is the suggestion of some toxicity. The average control weight (which was slightly higher than that for exposed animals on the final date) was markedly depressed by one animal which weighed only 4.75 kg on 12-21-83; the other four controls weighed 6.5 kg or more. Among exposed dogs, 36% (4 out of 11) weighed less than 6 kg on the same date.

The Toxicology Branch has no reason to revise its conclusions of March 13, 1984 with respect to the precautionary labeling for the Hartz Rabon dog collar.

It is recommended that in the future the registrant should submit protocols to the Agency for review and comment before initiation of studies of this nature.

Data Evaluation Report:

D'Ver, A.S. V.M.D. Final Report. Effects of the Use of An SD-8447 Collar on Puppies. Hartz Protocol #83-1. White Eagle Study No. 137, dated July 3, 1984.

Data Evaluation Report

Test Material: Presumably a Rabon dog collar, identified only as SD-8447 dog collar.

Citation:

D'ver, A.S. V.M.D. Effects of The Use of An SD-8447 Collar on Puppies. Hartz Protocol #83-1. White Eagle Study No. 137. Study conducted by White Eagle Laboratories, Inc. 2003 Lower State Road, Doylestown, PA 18901. Study dated July 3, 1984. Received at EPA 7-13-84; in Acc. 253946.

Reviewed by:

Byron T. Backus Byron T. Backus 08/16/84
Toxicologist

Core Classification: Invalid

Tox. Category: N/A

Conclusions:

The study is invalid. Some of the more obvious deficiencies include lack of identification (and percentage amount) of the active ingredient in the collar, and lack of data (sexes, which were sick and medicated with Chloramphenicol, total number of puppies in each litter, amount of collar) regarding the individual animals. Also, there were no RBC or plasma cholinesterase activity measurements, which would be considered appropriate for even such a weak cholinesterase inhibitor as Rabon (assuming it was the actual active). However, even with these data the study could not be considered relevant to the question of toxicity to newborn puppies, as the animals were already 4 weeks old when the collars were placed on them.

Even in this study there are possible indications of a toxic effect. The average control weight (which was slightly higher than that for exposed animals on 12-21-83) was markedly depressed by one animal which weighed 4.75 kg on that date. Among exposed animals, 36% (4 out of 11) weighed less than 6 kg on the same date.

Materials:

Eighteen beagle puppies, four weeks of age, unspecified as to sex. These puppies were part of six litters.

Placebo and SD-8447 collars.

Procedure:

Three puppies in each of 2 litters were fitted with placebo collars. Three puppies in each of 4 other litters were fitted with SD-8447 collars. An additional unspecified number of non-test puppies in each litter were also fitted with placebo collars. It is not explained how individual animals were identified.

Blood was taken from each puppy on 9-22-83, 10-21-83 and 12-21-83, at which time each was also weighed and given a complete physical examination.

Values for the following blood chemistry parameters (all presented as abbreviations) were obtained by some unspecified method:

GLUH	CL	PRO	UA
BUN	CO2	ALB	SGOT
CREA	AGAP	GLOB	SGPT
B/C	AP	CHOL	PK
NA	CA	TRIG	LDH
K	PO4	TBIL	

According to a letter of July 10, 1984 from the Hartz Mountain Corporation means were compared using t-test. However, the report from White Eagle Laboratories does not indicate that any statistical methods were employed.

Results:

One control pup and one exposed pup, as well as a non-study pup, died. They were diagnosed as having pneumonia. Several other puppies (no identification) were treated with Chloramphenicol for respiratory disease.

No irritation or other signs attributable to the collars were observed. At the conclusion of the study "all pups appeared to be healthy."

Blood chemistry values are reported as averages for controls and exposed animals, along with ranges for each date blood was taken. No individual data are reported. It is stated that AP values were higher in the exposed animals than in the controls, but that this difference had been present at the first blood sampling.

The average initial weight for the five controls which survived was 1.15 kg; for the 11 surviving exposed animals it was 1.16 kg. Three months later averages were 6.7 and 6.25 kg respectively. However, the control average was depressed by one animal which weighed only 4.75 kg; all other controls weighed 6.5 to 8 kg. Among the exposed animals 36% (4 out of 11) weighed less than 6 kg. The low-weight control animal was a littermate of the control which had died.

Discussion:

Cholinesterase data are completely lacking, along with pertinent information (sexes, litter sizes, which were treated with Chloramphenicol etc.) on the individual puppies. Blood chemistry data are presented only as group averages and ranges, both for controls and exposed animals, with no information as to individual values. In short, it is doubtful whether there is any significant relevant information in this study.

It is noteworthy that the protocol for this study appears to have been developed by the registrant, with no review or comment from this Agency.