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

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Blockade Cat 4X Application Study

TO: Mr. George LaRocca, PM 15
Registration Division (TS-767C)

FROM: Byron T. Backus, Toxicologist
Toxicology Branch (TS-769C)

THROUGH: Marcia van Gemert, Ph.D.
Section Head, Review Section III
Toxicology Branch (TS-769C)

and

Theodore M. Farber, Ph.D., D.A.B.T.
Branch Chief
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EPA Record No. 216481/216484

Project No. 8-0561

EPA Reg. Nos. 2596-114, 2596-115

Tox. Chem. 77A, 346

Action Requested:

Review a 4X application study on cats using Hartz Blockade.

Comments and Recommendations:

1. This study has been classified as core supplementary data. While no definite indications of toxicity were observed, the cumulative dose applied per individual cat in what was ostensibly a 4X application ranged from 19.9 to 54.9 grams, with a reported average of 31.5 grams. A single 1X application was from 4.2 to 17.4 grams. In the data previously reviewed (Toxicology Branch Review of September 24, 1987) the amounts (presumably a 1X dose level, as the animals were subsequently observed for product efficacy) sprayed on two cats were reported as 38 and 39.4 grams. It is therefore concluded that the 4X levels of this study were unreasonably low.

2. It is noted that the report includes a statement that treated animals were not observed to preen in the 14 days following treatment. This results in additional uncertainty as to the safety of this product (are there some cats that would preen no matter how bad it tastes?).

Reviewed by: Byron T. Backus Byron T. Backus 05/03/88
Section 3, Tox. Branch (TS-769C)
Secondary Reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) M. van Gemert 5/3/88

DATA EVALUATION REPORT I

STUDY TYPE: Domestic animal safety - cat TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: 405317-01 MRID NO.: 40531701

TEST MATERIAL: Blockade

SYNONYMS: Deet + Pydrin

STUDY NUMBER(S): Hartz Test No. 1002

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: [redacted]

NOTE: In the report which is not labeled confidential, the registrant has deleted the name of the laboratory at which this study was conducted. The name of the laboratory (and the personnel involved) is given in material which is labeled confidential.

TITLE OF REPORT: Domestic Animal Safety: Effect of a 4X Treatment on Cats

AUTHOR(S): [redacted]

REPORT ISSUED: February 21, 1988

CLASSIFICATION: Core Supplementary Data

CONCLUSIONS:

1. This study has been classified as core supplementary data. While no definite indications of toxicity were observed, the cumulative dose applied per individual cat in what was ostensibly a 4X application ranged from 19.9 to 54.9 grams, with a reported average of 31.5 grams. A single 1X application was from 4.2 to 17.4 grams. In the data previously reviewed (Toxicology Branch Review of September 24, 1987) the amounts (presumably a 1X dose level, as the animals were subsequently observed for product efficacy) sprayed on two cats were reported as 38 and 39.4 grams. It is therefore concluded that the 4X levels of this study were unreasonably low.

2. It is noted that the report includes a statement that treated animals were not observed to preen in the 14 days following treatment. This results in additional uncertainty as to the safety of this product (are there some cats that would preen no matter how bad it tastes?).

A. MATERIALS:

1. Test compound: Test sample #8340, obtained from a pallet of product manufactured 13 March 1987, production lot No. MR10727. Analysis showed an average of 10.16% Deet and 0.095% Fenvalerate (label declaration: 10.0% Deet; 0.110% Fenvalerate).

2. Test animals: A total of 48 male and female cats, consisting of a mixture of short and long-hairs, a few with Persian or Siamese ancestry. Ages ranged from 1-5 years, and weights (at the start of the study) from 4-13 lbs. The source of these animals is not reported.

B. STUDY DESIGN:

1. Animal assignment: Not reported.

2. Test material exposure: Each animal in one group of 19 males and 17 females (group A) was sprayed according to Blockade label directions until its coat was visibly wet. Another application was made when the cat's coat was dry (approximately one hour later), and so on until a total of 4 applications had been made in the period of approximately 3.5 hours. "Careful records of dosage amounts were maintained." The animals were then observed during the next 14 days.

   Each cat in a second group of 10 females and 2 males (group B) was also sprayed 4 times as above, and was then subsequently sprayed once with the product 10 days later to determine whether it had developed hypersensitivity to the product.

   "A method had to be developed for humanely handling the animals to avoid undue stress while still protecting the handlers from the animal's teeth and claws. It was determined that containing the animal within a large nylon fishnet afforded protection to the handlers without harming or frightening the animal. The use of this net did not impede the total body coverage required for treatment."

3. Quality assurance: there is a Quality Assurance Unit Statement dated 2/23/88 on p. 15 of the report. The signature is present on material in the confidential file.

C. METHODS AND RESULTS:

1. Observations:

   "The animals were carefully observed during the 4X treatment period (approximately 3 1/2 hours), hourly during the first 8 hours following the last treatment and at least once a day for 14 days after treatment."

Results:

From p. 7:

"No treatment related toxicity of any kind was observed in any of the test animals...the appetite of each cat remained normal throughout the test period."

"The only effect noted was salivation in cat #49 (Group A). This salivation started after the first spraying, decreased by the third spraying and had ended by the fourth spraying... It was thought to be caused by either the physical excitement of the restraint in a net...or by agitation due to the physical parameters associated with the aerosol spray, i.e. hissing, cold mist, etc."

"None of the 12 cats in Group B, treated 10 days after the initial 4X exposure, exhibited any treatment related effects. There were no signs of hypersensitivity in any of the animals."

"It should be noted that, although cats are known to preen, these animals were not observed preening after treatment with this product, or during the 14 day observation period. Therefore, potential toxicity via ingestion would be minimal. It is believed that the animals disliked the taste of the product and this inhibited their natural preening habits."

2. Animal weights:

From p. 8: "The weight of each test animal remained basically constant over the period of the test. With the exception of one cat which gained two pounds, no cat gained or lost more than one pound during the test."

3. Dosage applied:

From p. 8: "The average total amount of product sprayed on each animal (Groups A and B combined) during the course of the 4X treatment (over a period of approximately 3 1/2 hours) was 31.5 grams. The range was from a low of 19.9 total grams to a high of 54.9 grams. The animals in Group B, which received the additional treatment, were exposed to an average total amount of 33.4 grams of product over the course of both the 4X and the additional treatment."

"The average amount of test material versus body weight applied to each of the 48 test animals during each individual application...was 2.69 g/kg of body weight for a total average 4X application rate of 10.76 g/kg body weight during a 3 1/2 hour period. The 4X application dosage range was 6.78 to 15.04 g/kg..."

D. DISCUSSION:

The most serious problem with this study - and the reason it is classified as core supplementary data - is the relatively low exposure that these cats received, even at what was ostensibly a 4X dosage level. The mean cumulative dosage in the 4X treatment is reported as 31.5 grams.

In a previously submitted study (report issued 9/29/86; title: Hartz Mountain Feline Repellent Study Aerosol Spray Lot No. 7683) exposure data were provided for two cats. One received a single dose of 38 grams of this product, and another received a single dose of 39.4 grams. No information was given as to body weight, sex or approximate age of either of these cats. There was no indication that these cats received anything other than a 1X dose, especially as the reporting indicated that the product was efficacious at this dose level (there is no indication that the product was tested for efficacy at a lower dose level). A copy of the DER for this previously submitted study is appended.

It is noted that this previously submitted study was conducted at [redacted] the same laboratory subsequently conducting the "4X" study.

The report also includes a statement that treated animals were not observed to preen in the 14 days following treatment. This results in additional uncertainty as to the safety of this product (are there some cats that would preen no matter how bad it tastes?) even at the dose level at which it was tested.

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Reviewed by: Byron T. Backus Byron T. Backus 9/21/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) MvanGemert 9/21/87

DATA EVALUATION REPORT X

STUDY TYPE: Dermal Exposure - Cat TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: not assigned MRID NO.: not given

TEST MATERIAL: Diethyl toluamide (10%), and Fenvalerate (0.10%)

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: not given

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: [redacted]

TITLE OF REPORT: Hartz Mountain Feline Repellent Study Aerosol Spray Lot No. 7683

AUTHOR(S): [redacted]

REPORT ISSUED: 9/29/86

CLASSIFICATION: Core Supplementary

CONCLUSION:

1. No adverse reactions were observed in two cats which were sprayed once with the Blockade formulation. One cat was sprayed with 38 gms of formulation, the other with 39.4 grams. However, no further information (body weights, sex, approximate age) is reported for these two animals. Because only two animals were sprayed, the lack of information regarding these animals, as well as the fact that the test material was applied only at what was presumably a "normal" use exposure level, the value of this study is extremely limited.

2. Since the number of fleas on sprayed animals was considerably lower than that for control animals at 24 days, it is concluded that one or both actives in the Blockade formulation were still present on at least part of the animal's body at this time.

A. MATERIALS:

1. Test compounds: Sample #7683 identified as containing 0.11% technical (90%) fenvalerate and 10.0% DEET.

2. Test animals: Species: cat, Strain: no information provided; source: not reported; weight range: not reported. Sexes: not reported.

B. STUDY DESIGN:

1. Animal assignment: Two cats were sprayed with Blockade, and two cats served as controls (it is not certain whether these cats were simply not sprayed, or if they were sprayed with a placebo formulation). One of the cats sprayed with 38 gms of Blockade, the other was sprayed with 39.4 gms.

2. There is no Quality Assurance Statement, nor is there any indication that the lab performing the study adheres to GLP.

C. Observations:

There is no indication as to when or how frequently the cats were observed for possible signs of toxicity.

Results: "Neither of the treated cats showed any signs of drug induced toxicity following treatment."

D. DISCUSSION

The value of this study is limited, as the spray was applied at what is presumably the "normal" use exposure to only two cats (of unspecified sex, weight and age). The major points of interest from a toxicologic standpoint are that one animal received 38 gms and the other received 39.4 gms, and that apparently one or both actives was still present on the cats in sufficient amount(s) to be still efficacious 24 days after spraying.