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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SEP 24 1987

MEMORANDUM

SUBJECT: BLOCKADE cat and dog sprays

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
Toxicology Branch (TS-769C)

EPA Record Nos. 197405, 197776

Project No. 7-0976

Tox. Chem. 346, 77A

EPA Reg. Nos. 2596-114 Hartz Blockade for Cats
2596-115 Hartz Blockade for Dogs

Action Requested:

Review and comment on toxicity data (series of acute studies, dog and cat exposure studies) submitted for the Blockade formulation. In a previous expedited memorandum, it was noted that a comprehensive review of these data had yet to be made.

Comments and Recommendations:

1. The acute oral LD_{50}, acute dermal LD_{50}, dermal sensitization, primary eye and dermal irritation studies have been classified as core minimum data. The remainder (acute inhalation LC_{50}, three dog exposure and two cat exposure studies) have been classified as core supplementary data.

2. Although the oral LD_{50} was calculated as 6700 mg/kg for both sexes, from the female data (2/5 mortalities at 5 gm/kg, 3/5 at 6 gm/kg, all dying at 7 gm/kg and above) it appears that the 95% confidence limits would include values of less than 5 gm/kg. The products should therefore be labeled in toxicity category III in terms of oral hazard potential.

3. The Toxicology Branch expresses concern that effects were noted in all animals in the oral LD_{50} study. At 5 gm/kg (the lowest dose given) there was "moderate to severe ataxia" in all animals, beginning about 5 minutes after ingestion.

4. The products are in toxicity category III in terms of potential eye hazard, but there is no precautionary (or statement of practical treatment) labeling reflecting this.

5. The cat exposure studies (in which a total of 3 animals were sprayed) are clearly inadequate to demonstrate that a reasonable margin of safety exists with the "normal use" of the cat product. The only value of these studies is that they indicate an approximate dosage level (37-38 gm cat) at which adverse effects may not occur. From some of the adverse incident reports which the Agency has received mortalities have occurred following dosage at slightly above 100 gm/cat.

6. The three dog exposure studies are also inadequate to demonstrate the safety of the formulation, particularly as the animals were sprayed only at the "1X" level. The Toxicology Branch is concerned about the occurrence of a few incidents of emesis (2/160 in one study) and salivation (occuring 3 times in 136 sprayings) in another study. These possible symptom, occurring presumably as a result of a "1X use exposure" to the product, suggest that there may be an inadequate margin of safety between a normal use exposure and the level at which symptoms could be expected to occur.

7. The Toxicology Branch recommends that oral studies be conducted with dogs and cats to determine dosage levels at which no toxic effects occur. Further, the registrant should conduct studies which show how much of the product remains as a residue after evaporation, and what the composition of this residue is. It is noted that as additional information is received it will probably be necessary to request additional testing.

2

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) M. van Gemert 9/21/87

DATA EVALUATION REPORT I

STUDY TYPE: Acute Oral LD_{50} - Rat

TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: not assigned

MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 14.286%, Fenvalerate (97% active) 0.148%.

SYNONYMS: Hartz Mountain

STUDY NUMBER: C-55106-00

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Leberco Testing, Inc.
123 Hawthorne St.
Roselle Park, NJ 07204-0206

TITLE OF REPORT: Acute oral toxicity in rats - the Hartz Mountain Corporation - sample #7628

AUTHOR(S): Rothstein, E. C.

REPORT ISSUED: 8/21/86

CLASSIFICATION: Core Minimum

CONCLUSION:

1. The study presents only a combined (both sexes) oral LD_{50} for this test material. It seems obvious, from the data, that females were more susceptible than males (at doses of 7 gm/kg and above 15/15 females died, while only 6/15 males did so, also, 5/10 females at 5 and 6 gm/kg died, while only 2/10 males did so). While the data would probably "show" a female oral LD_{50} greater than 5 gm/kg (2/5 died at 5 gm/kg; 3/5 died at 6 gm/kg) the 95% confidence limits would be such that the product would "straddle" toxicity categories III and IV in this respect. The precautionary labeling for this product in terms of its oral hazard potential would then be that for toxicity category III.

2. An additional concern is that even at the lowest dose (5 gm/kg) all animals showed effects ("...moderate to severe ataxia within 5 minutes").

A. MATERIALS:

1. Test compound: Sample #7628, identified as a clear colorless liquid with a density of 1 ± 0.05 g/ml. According to the last page of the report (attached at/by Hartz Corporation?) the actives in test sample #7628 consisted of Fenvalerate (97% active) 0.148% and diethyl toluamide 14.286%. This is a concentrate (without the propellents) for the Blockade formulations.

2. Test animals: Species: rat, Strain: Sprague-Dawley derived, source: Taconic Farms, Inc. Germantown, NY 12526. Age at receipt: 7 weeks; weights at receipt: males 175-200 gms; females 150-175 gms. Weight range in the study: males 232-290 gms, females 161-198 gms.

B. STUDY DESIGN:

1. Animal assignment: not specified, except that the animals used had been acclimated for at least 7 days prior to testing.

2. Dosage levels: A Group of 5 male and 5 female rats was initially dosed (syringe and intubation tube) at 5 gm/kg. When 2 mortalities occurred, groups of 5 males and 5 females were dosed at 6, 7, 9 and 10 gm/kg.

3. Animals received "standard laboratory feed for rats" and water ad libitum.

4. Statistics - A combined (both sexes) oral LD_{50} was calculated using what appears to be a least difference of squares method.

5. A signed and dated (8-21-86) Quality Assurance Unit Statement is provided on the last text page of the report.

C. METHODS AND RESULTS:

1. Observations

Animals were observed daily for signs of toxicity and mortality for 14 days after dosage. Survivors were then sacrificed with CO_2 (presumably asphyxiation) and gross necropsies were performed.

Toxicity: All rats exhibited ataxia, even at the lowest dosage level (5 gm/kg). At least some animals became cataleptic even at the lowest dosage levels.

Mortality:

Dosage level	Incidence mortality/animals dosed Males	Females
5 gm/kg	0/5	2/5
6 gm/kg	2/5	3/5
7 gm/kg	0/5	5/5
9 gm/kg	2/5	5/5
10 gm/kg	4/5	5/5

Deaths occurred up to 5 days after dosage.

2. Body weight: Survivors gained weight.

3. Necropsies: Findings in some of the mortalities included bloating of the stomach and intestines. For a number of the animals which died "no necropsies were performed since autolysis had already occurred."

4. The combined (both sexes) oral LD50 was calculated as 6700 mg/kg, with 95% confidence limits of 5668 to 7919 mg/kg.

D. DISCUSSION

While the study is classified as core minimum data, there are a number of concerns that this reviewer has regarding the lack of separate calculations for male and female oral LD_{50} values. From the data it appears that females are more susceptible than males (at doses of 7 gm/kg and above 15/15 females died, while only 6/15 males did so, also, 5/10 females at 5 and 6 gm/kg died, while only 2/10 males did so). The conclusion of this reviewer is that while the data would indicate a female oral LD_{50} greater than 5 gm/kg, the 95% confidence limits would be such that the product would "straddle" toxicity categories III and IV, and the appropriate labeling for this product in terms of its oral hazard potential would be that for toxicity category III.

Another concern is the occurrence of symptoms ("moderate to severe ataxia") in all rats receiving even the lowest dose given (5 gm/kg). No information is given as to a dose level at which there were no observable effects.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D. M. van Gemert 9/21/87
Section 3, Tox. Branch (TS-769C)

DATA EVALUATION REPORT II

STUDY TYPE: Acute Dermal LD_{50} - Rabbit TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: not assigned MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 14.286%, Fenvalerate (97% active) 0.148%.

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: Assay no. 606122

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Leberco Testing, Inc.
123 Hawthorne St.
Roselle Park, NJ 07204-0206

TITLE OF REPORT: Acute dermal toxicity in rabbits - the Hartz Mountain Corporation - sample #7628

AUTHOR(S): Rothstein, E. C.

REPORT ISSUED: 8/5/86

CLASSIFICATION: Core Minimum Data

CONCLUSION:

1. The study is acceptable in demonstrating the product is in toxicity category III by this exposure route (dermal LD_{50} > 2 gm/kg). However, the text suggests that weight losses in five rabbits may have been due to diarrhea, but the observational notes indicate this was observed only in a single rabbit (#19) during the 7 days following dosage (it is noted that this particular rabbit showed the greatest weight loss).

A. MATERIALS:

1. Test compound: Sample #7628, identified as a clear colorless liquid with a density of 1 ± 0.05 g/ml. According to the last page of the report (attached at/by Hartz Corporation?) the actives in test sample #7628 consisted of Fenvalerate (97% active) 0.148% and diethyl toluamide 14.286%. This is a concentrate (without the propellents) for the Blockade formulations.

2. Test animals: Species: rabbit, Strain: New Zealand White, source: Gingrich Animal Supply, Fredericksburg, PA 17026. Initial weight range: 2.0-3.0 kg.

B. STUDY DESIGN:

1. Animal assignment: not specified, except that the animals used had been acclimated for at least 7 days prior to testing.

2. Dosage levels: 5 males and 5 females were given a 24-hour occluded dermal exposure to 2 gm/kg of the test material, during which time the animals were restrained in stocks. "After the 24 hour exposure period the patches and residual test material were removed."

3. Animals received "standard laboratory feed for rabbits" and water ad libitum.

4. A signed and dated (8-5-86) Quality Assurance Unit Statement is provided on the last text page of the report.

C. METHODS AND RESULTS:

1. Observations

"Animals were examined within 30-60 minutes after patch removal and then daily for 14 days."

There is no indication as to how the rabbits were sacrificed. According to the results section: "No gross abnormalities were observed in any of the rabbits upon autopsy."

Toxicity: Some local skin effects (minor erythema and/or edema) were noted in some of the subjects. It is noted in the results section that "five rabbits lost weight... This weight loss may be due to diarrhea which persisted for 7 days." A check of the xeroxed raw data, however, seems to indicate that "diahrrea" was observed only in one rabbit (#19), which showed the greatest weight loss.

Mortality: No rabbits died as a result of exposure at this dose level.

2. The dermal LD50 is greater than 2 gm/kg.

D. DISCUSSION

The study is acceptable. However, there is a question as to whether diarrhea was actually observed in most (all?) rabbits, or actually occurred in only the single rabbit (#19) with the greatest weight loss.

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

DATA EVALUATION REPORT III

STUDY TYPE: Primary Dermal Irritation - Rabbit TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 14.286%, Fenvalerate (97% active) 0.148%.

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: Assay no. 605311

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Leberco Testing, Inc.
123 Hawthorne St.
Roselle Park, NJ 07204-0206

TITLE OF REPORT: Primary Dermal Irritation Study - the Hartz Mountain Corporation - sample #7628

AUTHOR(S): Rothstein, E. C.

REPORT ISSUED: 6/26/86

CLASSIFICATION: Core Minimum Data

CONCLUSION:

1. The study is acceptable. The product concentrate is in toxicity category IV in terms of dermal irritation potential.

A. MATERIALS:

1. Test compound: Sample #7628, identified as a clear colorless liquid with a density of 1 ± 0.05 g/ml. According to the last page of the report (attached at/by Hartz Corporation?) the actives in test sample #7628 consisted of Fenvalerate (97% active) 0.148% and diethyl toluamide 14.286%. This is a concentrate (without the propellents) for the Blockade formulations.

2. Test animals: Species: rabbit, Strain: New Zealand White, source: Gingrich Animal Supply, Frdericksburg, PA 17026. Initial weight range: 2.0-3.0 kg.

B. STUDY DESIGN:

1. Animal assignment: not specified, except that the animals used had been acclimated for at least 7 days prior to testing.

2. Dosage levels: 6 females were given a 4-hour occluded dermal exposure to 0.5 ml of the test material at one unabraded site (at which the hair had been clipped), during which they were restrained in stocks. Animals were examined (and scored for irritation) at 4, 24, 48 and 72 hours.

3. Animals received "standard laboratory feed for rabbits" and water ad libitum.

4. A signed and dated (6-26-86) Quality Assurance Unit Statement is provided on the last text page of the report.

C. METHODS AND RESULTS:

1. Observations

"Animals were examined within 30-60 minutes after patch removal and then daily for three days." Sites were scored at 4, 24, 48 and 72 hours.

Results: No irritation was noted at any time in any of the six rabbits.

2. The PDIS was 0.00.

D. DISCUSSION

The study is acceptable. The formulation is in toxicity category IV in terms of its dermal irritation potential.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D. M. van Gemert 9/4/87
Section 3, Tox. Branch (TS-769C)

DATA EVALUATION REPORT IV

STUDY TYPE: Acute Inhalation LC_{50} - Rat TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 14.286%, Fenvalerate (97% active) 0.148%.

SYNONYMS: Hartz Mountain

STUDY NUMBER: Assay no. 606121

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Leberco Testing, Inc.
123 Hawthorne St.
Roselle Park, NJ 07204-0206

TITLE OF REPORT: Acute ~~oral~~ inhalation toxicity in rats - the Hartz Mountain Corporation - sample #7628

AUTHOR(S): Rothstein, E. C.

REPORT ISSUED: 8/8/86

CLASSIFICATION: Core Supplementary Data

CONCLUSION:

1. The study suggests a low hazard potential for the product by inhalation exposure (rat LC_{50}> 5 mg/liter for 4-hr exposure. However, while gravimetric data suggest that the rats were exposed to more than 5 mg/l of some material, there is a question as to what exactly rats were exposed to, as no analytical data (concentration of diethyl-m-toluamide and/or fenvalerate) were developed. Also, the material tested was the concentrate, rather than the actual product (concentrate + propellent) to which exposure occurs. As a result, there is some uncertainty as to how adequately this study reflects potential inhalation exposure.

A. MATERIALS:

1. Test compound: Sample #7628, identified as a clear colorless liquid with a density of 1 + 0.05 g/ml. According to the last page of the report (attached at/by Hartz Corporation?) the actives in test sample #7628 consisted of Fenvalerate (97% active) 0.148% and diethyl toluamide 14.286%. This is a concentrate (without the propellents) for the Blockade formulations.

2. Test animals: Species: rat, Strain: Sprague-Dawley derived, source: Taconic Farms, Inc. Germantown, NY 12526. Age at receipt: 7 weeks; weights at receipt: males 175-200 gms; females 150-175 gms. Weight range in the study: males 243-265 gms, females 186-209 gms.

B. STUDY DESIGN:

1. Animal assignment: "Animals placed on test were randomly assigned to dose groups." Animals used had been acclimated for at least 7 days prior to testing.

2. Dosage levels: The rats were exposed for 4 hours to a measured concentration of 5 mg/liter (nominal value: 19.02 mg/liter).

3. Animals received "standard laboratory feed for rats" and water ad libitum with deprivation during exposure.

4. A signed and dated (8-8-86) Quality Assurance Unit Statement is provided on the last text page of the report.

C. METHODS AND RESULTS:

1. Observations

There is no indication within this report that rats were observed during the actual exposure period. Rats were subsequently observed twice daily for signs of toxicity and mortality for "5 days a week for the first week after exposure and once daily thereafter."

Toxicity: "All ten animals appeared normal throughout the 14 day observation period."

Mortality: All rats survived the 14-day post-exposure period.

2. Post-sacrifice necropsy: Rats were sacrificed ("CO_2 overdose") and were grossly necropsied.

Results: "No gross abnormalities were observed in any of the animals."

3. Body weight: All animals gained weight.

4. Measurement of exposure parameters: the nominal concentration ("theoretical atmospheric concentration") was 182.6 gms of test material ÷ total volume of air (9600 liters) = 19.02 mg/l. Test material concentration was calculated by pulling 20 liter samples of chamber atmosphere through glass fiber filters at 30, 120 and 210 minutes, measuring increases in filter weight, and assuming these weight increases were due to the test material alone. From this an "air concentration" mean of 5.36 mg/l was calculated. According to three measurements from the cascade impactor system concentrations of the particulate matter in the system were 1.1949, 1.1487 and 1.2228 mg/m^3 at these respective sampling times. From the data presented it appears that approximately 50% of the particulate matter was 6.4 u or larger.

D. DISCUSSION

The study suggests a low hazard potential for the product by inhalation exposure (rat LC_{50}> 5 mg/liter for 4-hr exposure. However, while gravimetric data suggest that the rats were exposed to more than 5 mg/l of some material, there is a question as what exactly the rats were exposed to, as no analytical data (concentration of diethyl-m-toluamide and/or fenvalerate) were developed. Also, the material tested was the concentrate, rather than the actual product (concentrate + propellent) to which exposure occurs. Because of the resulting uncertainty then as to how adequately this study relates to actual exposure, the classification is core supplementary.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D. M. van Gemert 9/21/87
Section 3, Tox. Branch (TS-769C)

DATA EVALUATION REPORT V

STUDY TYPE: Primary Eye Irritation - Rabbit

TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER:

MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 10.00%, Fenvalerate (90% active) 0.11%.

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: Assay no. 611189

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Leberco Testing, Inc.
123 Hawthorne St.
Roselle Park, NJ 07204-0206

TITLE OF REPORT: Primary Eye Irritation Study - The Hartz Mountain Corporation - sample #8060

AUTHOR(S): Rothstein, E. C.

REPORT ISSUED: 2/2/87

CLASSIFICATION: Core Minimum Data

CONCLUSION:

1. The study is acceptable. The product is in toxicity category III in terms of eye irritation potential.

2. Precautionary labeling for the Hartz dog and cat Blockade products should be revised to include an appropriate eye hazard statement, as well as the corresponding practical treatment for this route of exposure.

A. MATERIALS:

1. Test compound: Sample #8060, identified as a clear colorless liquid with a pH of 5.5. According to the last page of this report (attached at/by Hartz Corporation?) the actives in this sample consisted of 0.11% Fenvalerate (90% active) and 10.00% diethyl toluamide 14.286%. This is the formulation (including propellents) for the Blockade cat and dog products.

2. Test animals: Species: rabbit, Strain: New Zealand White, source: Gingrich Animal Supply, Frdericksburg, PA 17026. Initial weight range: 2.0-3.0 kg.

B. STUDY DESIGN:

1. Animal assignment: not specified, except that the animals used had been acclimated for at least 7 days prior to testing.

2. Dosage levels: 6 females each received a one-second spray in one eye. None of the eyes were washed.

3. A signed and dated (1-16-87) Quality Assurance Unit Statement is provided on page 10. There is a signed Good Laboratory Practice Statement on p. 3.

C. METHODS AND RESULTS:

1. Observations

Eyes were examined and scored at 1, 2, 3, 4, 7, 8 and 10 days.

All eyes showed some conjunctival irritation with chemosis and discharge at 24 hours; 5/6 also showed some corneal involvement at this time. By day 8 all eyes were clear.

D. DISCUSSION

The study is acceptable. The formulation is in toxicity category III in terms of its eye irritation potential. The label should be revised accordingly.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/82
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) Marcia van Gemert 9/21/82

DATA EVALUATION REPORT VI

STUDY TYPE: Dermal Sensitization - Guinea Pig

TOX. CHEM. NO.: 346, 77A

ACCESSION NUMBER: not assigned

MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 14.286%, Fenvalerate (97% active) 0.148%

SYNONYMS: Hartz Mountain

STUDY NUMBER: 86316-1

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: Consumer Product Testing
1275 Bloomfield Ave.
Fairfield, NJ 07006

TITLE OF REPORT: Guinea Pig Sensitization - Buehler

AUTHOR(S): Nitka, S., Palankar, A. L.

REPORT ISSUED: 8/07/86

CLASSIFICATION: Core Minimum

CONCLUSION:

1. There was no evidence of dermal sensitization in this study. The study is acceptable in defining a low sensitization potential for this product formulation.

A. MATERIALS:

1. Test compound: Sample #7628A, identified only as containing 0.148% technical (97%) fenvalerate and 14.286% diethyl toluamide, according to the last page of the report (attached at/by Hartz Corporation?).

2. Test animals: Species: guinea pig, Sex: male; Strain: Hartley, source: "a suitably licensed breeding farm."

B. STUDY DESIGN:

1. Animal assignment: not specified, except that the animals had been checked upon receipt and prior to testing for evidence of poor health. They had been acclimated for 7 days prior to testing.

2. Dosage level: After a preliminary study in which a single test animal received one 6-hr occluded dermal exposure to 0.5 ml of the test material and showed no subsequent dermal irritation, the material was tested undiluted. The induction schedule consisted of 9 applications of the test material over a 3-week period, a resting period of 2 weeks, and then application of the test material at both the original (induction) application site and a previously unused site.

3. A signed (8-21-86) Quality Assurance Unit Summary appears on page 3 of the report.

C. METHODS AND RESULTS:

1. Observations

There was no irritation noted at any site after any of the induction or challenge applications. One animal died between the end of the induction and the challenge period. A necropsy revealed: "fibrous tissue in the thoracic cavity, a common infection in large guinea pig colonies."

D. DISCUSSION

The study is acceptable as core minimum data. There was no indication of a dermal sensitization reaction resulting from exposure to this formulation.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) M. van Gemert 9/29/87

DATA EVALUATION REPORT VII

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

ACCESSION NUMBER: not assigned MRID NO.: not given

TEST MATERIAL: Diethyl toluamide 10.00%, Fenvalerate 0.92 and 0.103%.

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: not given

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: [redacted]

TITLE OF REPORT: Hartz Mountain Toxicity Study Aerosol Sprays Lot Nos. 7612 and 7614.

AUTHOR(S): [redacted]

REPORT ISSUED: 6/29/86

CLASSIFICATION: Core Supplementary

CONCLUSION:

1. While the study indicates adverse effects from exposure to the dermal spray were relatively minor (40 dogs were sprayed 4 times at intervals of 5 days, and there were two incidents of "mild emesis" out of the 160 total sprayings), no information is presented as to the actual dosage level of test material that was applied to each of the dogs.

2. It seems doubtful that the dogs were sprayed at any level higher than normal use (whatever that means), so it is unlikely that the study provides any information as to what safety factor is associated with routine use of the product (although the occurrence of occasional emesis is disquieting).

A. MATERIALS:

1. Test compounds: Sample #7612, identified as containing 0.103% fenvalerate and 10.0% Deet; sample #7614, identified as containing 0.92% fenvalerate and 10.0% Deet.

2. Test animals: Species: dog, Strain: a variety of breeds and mixtures; source: not reported; weight range 8-58 lbs. Presumably a mixture of sexes, but only two of the animals can be identified (as it is noted that they were nursing puppies) as females

B. STUDY DESIGN:

1. Animal assignment: "Forty dogs were divided into two groups with twenty in each group. The dogs in each group were sprayed two separate times with one sample. Then the groups were switched, and the dogs were sprayed two separate times with the other sample."

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

C. Observations:

Dogs were observed, although there is no indication as to the frequency of observation.

Results: Two dogs vomited, one within 2 hours of exposure to the #7614 formulation, and the other within 2 hours of exposure to the #7612 formulation. No other "side reactions" are reported, although there is no indication as to how long the dogs were observed, or whether they were even observed except on the days that they were treated. There was no mortality. Only a single (initial?) body weight is reported for each dog.

Two dogs are reported as having nursing puppies. "During treatments their udders were thoroughly sprayed, and the puppies were never restrained from nursing. No side reactions were ever observed in any of the puppies."

D. DISCUSSION

The value of this study is extremely limited. No dosages (either in terms of grams applied/animal or grams applied/body weight basis) are reported, so it is difficult to relate the findings of the study to potential effects which might occur from overspraying. Also, it is not immediately apparent whether dogs were observed only at (within?) the 2-hr period after spraying, what the sexes of most of the animals were, or their approximate ages.

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) M van Gemert 9/21/87

DATA EVALUATION REPORT VIII

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

ACCESSION NUMBER: MRID NO.: not given

TEST MATERIAL: Diethyl toluamide (presumably 10%), and some amount (presumably <1%) Fenvalerate

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: not given

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: [redacted]

TITLE OF REPORT: Hartz Mountain Toxicity Study Aerosol Sprays Lot No. 7573

AUTHOR(S): [redacted]

REPORT ISSUED: 4/20/86

CLASSIFICATION: Core Supplementary

CONCLUSION:

1. Salivation is noted in the text as having occurred on 3 occasions out of 136 sprayings. It occurred in one dog twice and in one dog once. However, in the summary table it is stated there were no side reactions. In this study 50 dogs were sprayed a total of 136 times with the contents of 50 cans. If each can contained 7 ounces of spray then the average application was 2.57 ounces (= 73.0 grams).

2. Since dogs were only sprayed at "normal use" (whatever that means), it is unlikely that the study provides any particularly useful information defining what sort of safety factor is associated with routine use of the product. The occurrence of salivation is disturbing, particularly as this symptom has been frequently reported in the incidents involving Blockade.

A. MATERIALS:

1. Test compounds: Sample #7573, with no identification as to the percentage actives. Other Blockade spray studies utilized

formulations containing 10.0% Deet and 0.10-0.92% Fenvalerate.

2. Test animals: Species: dog, Strain: a variety of breeds and mixtures; source: not reported; weight range 12-56 lbs. Presumably a mixture of sexes, but only one of the animals can be identified (as it had two puppies following the second treatment) as a female.

B. STUDY DESIGN:

1. Animal assignment: Eighteen dogs were sprayed 4 times (with one week intervals between sprayings) and 32 dogs were sprayed twice (with a one week interval between sprayings). It is noted that a total of fifty aerosol cans were used in the study and a total of 136 treatments were administered.

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

C. Observations:

Dogs were observed, although there is no indication as to whether observations were limited to the periods immediately after spraying (and if so, for how long).

Results: It is reported in the results section that two dogs showed salivation during treatment. "In one dog it occurred twice and in another dog once. As soon as these dogs were returned to their pen the salivation stopped." These dogs are not identified as to subject number, and the table listing treatment dates reports, for each application, no side reactions. A female delivered 2 healthy puppies four days after a second treatment, and it is reported that neither she nor the puppies had any side reactions to two subsequent treatments (applied to the mother only).

D. DISCUSSION

The value of this study is limited. It is disturbing that salivation is noted in the results section as having occurred on 3 occasions, particularly as this symptom has been reported as occurring in adverse reactions. The study does indicate that 50 cans yielded a total of 136 treatments, which suggests (assuming 7 ounces/can) that the average application was 2.57 ounces (= 73.0 grams).

Reviewed by: Byron T. Backus Byron T. Backus 9/18/87
Section 3, Tox. Branch (TS-769C)
Secondary reviewer: Marcia van Gemert, Ph.D.
Section 3, Tox. Branch (TS-769C) M. van Gemert 9/21/87

DATA EVALUATION REPORT IX

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

ACCESSION NUMBER: not assigned MRID NO.: not given

TEST MATERIAL: Diethyl toluamide (presumably 10%), and some amount (presumably <1%) of Fenvalerate.

SYNONYMS: Hartz Mountain Blockade

STUDY NUMBER: not given

SPONSOR: Hartz Mountain Corporation

TESTING FACILITY: [redacted]

TITLE OF REPORT: Hartz Mountain Toxicity Study Aerosol Sprays Lot Nos. 7654, 7655A and 7655B.

AUTHOR(S): [redacted]

REPORT ISSUED: 8/23/86

CLASSIFICATION: Core Supplementary

CONCLUSION:

1. No adverse reactions were reported in 70 dogs each of which was sprayed once with a Blockade formulation.

2. The value of this study is limited, as there is no indication of the average dosage applied to each dog, and the application rate was presumably that of a "normal use" of the product, which gives no indication as to what margin of safety might be present.

A. MATERIALS:

1. Test compounds: Samples #7574, 7655A and 7655B with no identification as to the percentage actives. Other Blockade spray studies have utilized formulations containing 10.0% Deet and 0.10-0.92% Fenvalerate. Sample 7654 is identified as "Blockade formula [redacted] while samples 7655A and 7655B are "Blockade formula."

2. Test animals: Species: dog, Strain: a variety of breeds and mixtures; source: not reported; weight range 10-52 lbs. Presumably a mixture of sexes.

B. STUDY DESIGN:

1. Animal assignment: Seventy dogs were each sprayed once. 36 were treated with lot no. #7654 (Blockade formulation [redacted] the other dogs were treated with lots no #7655A and #7655B ("Blockade formula").

"The treatment consisted of thoroughly spraying the entire surface of the dog's body except the face. No special effort was made to prevent the dogs from inhaling the vapors during the treatment. Also, the dogs were not prevented from licking themselves following treatment."

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

C. Observations:

"The animals were examined repeatedly for 24 hours after treatment for signs of irritations or toxicity."

Results: "None of these seventy dogs appeared to have any kind of side reaction following treatment, and their appetite remained good throughout the test period."

D. DISCUSSION

The value of this study is limited, as there is no indication as to the average amount of spray applied to each dog, and the application rate was presumably that of normal anticipated use, so there is no indication as to what margin of safety may be present.

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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.

Reviewed by: Byron T. Backus Byron T. Backus 9/11/87
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Secondary reviewer: Marcia van Gemert, Ph.D. Marcia van Gemert 9/21/87
Section 3, Tox. Branch (TS-769C)

DATA EVALUATION REPORT XI

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. 8262

AUTHOR(S): [redacted]

REPORT ISSUED: 7/5/87

CLASSIFICATION: Core Supplementary

CONCLUSION:

1. No adverse reactions were observed in a single cat which was sprayed once with the Blockade formulation. One cat was sprayed with an unspecified amount of Blockade and was then observed for 10 days. No further information (body weight, sex, approximate age) is reported for this animal. Because only one animal was sprayed, the lack of information regarding this cat, and because the test material was applied only at what was presumably a "normal" use application level, the value of this study is extremely limited.

2. Since the number of fleas on the treated cat was considerably lower than that for a control animal at 17 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 #8262 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. Sex: not reported.

B. STUDY DESIGN:

1. Animal assignment: One cat was sprayed with Blockade, and one cat served as a control (it is not certain whether this cats was simply not sprayed, or if it was sprayed with a placebo formulation). It is not indicated how much Blockade was sprayed on the treated cat.

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 cat was observed for possible signs of toxicity.

Results: "The treated cat showed no signs of drug induced toxicity following treatment."

D. DISCUSSION

The value of this study is extremely limited, as the spray was applied at what is presumably the "normal" use exposure to only one cat (of unspecified sex, weight and age). The major point of interest from a toxicologic standpoint is that apparently one or both actives was still present on this cat in sufficient amount(s) to be still efficacious 17 days after application.