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

CASWELL FILE
007683

JAN 18 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Caswell No.: 216A
RD Record No.: 254,073
HED Project No.: 0-0177

MEMORANDUM

SUBJECT: STARLICIDE® (DRC-1339; 3-chloro-p-toluidine. HCl) - Acute Toxicity Data Submitted Under MRID Nos. 41267205 and 41267206
EPA ID No. 56228-10

FROM: Irving Mauer, Ph.D., Geneticist
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1-8-90

TO: William H. Miller/Steve Palmateer, PM Team 16
Insecticide-Rodenticide Branch
Registration Division (H7505C)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

1/12/90

Registrant: US Department of Agriculture (APHIS)
Hyattsville, MD

Request

Review and evaluate the following two (2) acute toxicity studies to support the proposed use of subject pesticide as an avicide to control starling populations in feedlots:

1. Acute Toxicity to Selected Mammals for the Chemical, 3-Chloro-4-methylbenzeneamine hydrochloride (Compound DRC-1339; CPTH), completed at the USDA (APHIS) Wildlife Research Center, Denver, CO, Special Report No. 6, dated September 1989 (EPA MRID No. 41267205).

1

2. Acute Dermal Toxicity to Rabbit[s] for the Chemical, 3-Chloro-4-methylbenzeneamine hydrochloride (Compound DRC-1339; CPTH), performed at USDA (APHIS), Wildlife Research Center, Denver, CO, Special Report No. 7, dated September 1989 (EPA MRID No. 41267206).

TB Conclusions

Following are HED summary assessments of acute toxicity studies with compound DRC-1339 as reported by USDA/APHIS (detailed reviews are appended to this memorandum):

| Study | Reported Results | TB Evaluation |
|---|---|---|
| 1. Acute oral toxicity (Rat) | $LD_{50}$ (males) = 1770 mg/kg<br>$LD_{50}$ (females) = 1170 mg/kg | SUPPLEMENTARY |
| 2. Acute dermal toxicity (Rabbit) | $LD_{50}$ = 2680 mg/kg (males only) | SUPPLEMENTARY |
| 3. Primary dermal irritation (Rabbit) | PIS = 0.125 (for the 1% product)<br>0.54 (for the 10% product) | SUPPLEMENTARY |
| 4. Primary ocular irritation (Rabbit) | Reported not to be an irritant, but no supporting data provided. | INVALID |

Attachments (DERs)

2

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Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch I - IRS (H7509C)

DATA EVALUATION REPORT

007683

I. SUMMARY

MRID No.: 41267205
ID No.: 56228-10
RD Record No.: 254,073
Caswell No.: 216A
Project No.: 0-0177

Study Type: (81-1) Acute Oral ($LD_{50}$) Toxicity - Rat

Chemical: DRC-1339 [3-chloro-4-methylbenzeneamine hydrochloride]

Synonyms: STARLICIDE®; 3-chloro-p-toluidine. HCl (CPTH)

Sponsor: USDA (APHIS)
Hyattsville, MD

Testing Facility: Denver Wildlife Research Center (USDA, S&T)
Denver, CO

Title of Report: Acute Oral Toxicity to Selected Mammals for the Chemical, 3-Chloro-4-Methylbenzeneamine Hydrochloride.

Author: C. Edward Knittle

Study No.: (None)

Date of Issue: September 1989

TB Conclusions:

An $LD_{50}$ was calculated for CFW rats as 1770 mg/kg for males, 1170 mg/kg for females, based upon 1966 data.

Classification (Core-Grade):

SUPPLEMENTARY, since study does not meet current FIFRA data requirements; for labeling, however, test material is assessed as no worse than Toxicity Category III.

II. DETAILED REVIEW

A. Test Material - Compound DRC-1339 Concentrate; CPTH (as stated on submitted label)

Description: Crystalline powder
Batch (Lot): (Not stated)
Purity (%): 98
Solvent/Carrier/Diluent: Corn oil

B. Test Organism - Rodent

Species: Rat
Strains: CFW (albino)
Age: (Not stated)
Weights - Males: 134 to 140 g
Females: 90 to 110 g
Source: (Not stated)

C. Study Design (Protocol) - This study was designed to assess the acute oral toxicity potential of DRC-1339 concentrate when administered by gavage to rats (and other mammals).

This submission was declared as not conforming to the Agency's GLPs (40 CFR Part 160), since it is a summary of unpublished information (raw data) as well as published articles on file at the Denver Wildlife Research Center, generated before the implementation of 40 CFR Part 160.

D. Procedures/Methods of Analysis

1. Groups of five CFW rats (5 males, 5 females) per group were fasted overnight, then administered test compound once by oral gavage at doses of 313, 625, 1250, and 2500 mg/kg, and examined daily for 14 days (Tab No. 2585 in submission[1/]);

2. Groups of laboratory (Mus musculus) Swiss (white) mice (3 males, 3 females per group) were dosed orally by gavage at six acute dose levels of test article ranging from 500 to 2000 mg/kg (Tab No. 5142 of this submission[2/]). DRC-1399 was also assayed in

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1/Anonymous (1966). Toxicology of Compound 47676. (Unpublished). American Cyanamid Company.
2/Peoples, S.A. (1965) The Use of Toxicants in Starling Control. Joint Progress Report, Univ. of Cal. AG.EXPT.STA. (Wash DC) and Calif. Dept. Agric.

deer mice (Peromyscus maniculatus), as reported in a recent published survey (Tab 12495 of submission[3/]); for each of the 933 chemicals tested, ALDs (approximate oral lethal doses) were estimated by treating two to four animals with test article at geometrically-spaced dosages.

3. Groups of two dogs (one/sex/group, strain unspecified) were gavaged orally once at five dose levels of DRC-1399, ranging from 50 to 1000 mg/kg (Tab No. 2388[1/]).

4. In addition, a variety of other mammalian species had been treated with the test article, including farm animals, notably swine (as reported at Tab No. 11220 of the current submission[4/]). In the pig tests, two methods of administration were employed. In the first, groups of younger (2 to 4 mo) and older (4 to 6 mo) swine (4 males, 4 females, breed unspecified) were gavaged once with gelatin capsules containing 50 mg/kg DRC-1339, or by stomach tube with a solution of DRC-1339 in corn oil at the same dosage level, observed for 30 days, and necropsied. For the second method, six pigs were each fed five starlings (previously killed by DRC-1339 poisoning) blended in with their regular ration daily for 20 days; a control group received untreated starlings.

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3/E.W. Schafer and W.A. Bowles (1985) Acute Oral Toxicity and Repellency of 933 Chemicals to House and Deer Mice, Arch. Environ. Contam. Toxicol. 14; 111-129.

4/Caslick, J.W.; H.P. Pan; D.T. Harke; D.G. Decker and L.N. Lock (1972) Primary and Secondary Poisoning of Swine Treated with DRC-1399. (Unpublished). Final Report, Work Unit P-F-33-4. USFWS, Patuxent Wildlife Research Center, Laurel, MD (tests conducted at the Gainseville, FL Field Station).

E. Results - The following summary of acute oral toxicities[5/] was provided in this submission (detailed results follow tabulation):

| | Species/Strain | $LD_{50}$ (mg/kg)[6/] | TB Evaluation |
|---|---|---|---|
| 1. | Rat/CFW (albino) | Males = 1770 (no C.I.)<br>Females = 1170 (830 to 1640) | SUPPLEMENTARY |
| 2. | Mouse: | | |
| | Mus musculus/ (Strain not stated) | Combined = 2000 | -- |
| | Mus musculus/ ("White") | Combined > 1000 | -- |
| | Mus musculus/ Swiss | Combined = 960 | -- |
| | Peromyscus sp. | Combined = 1800 | -- |
| | P. maniculatus | Combined > 1600 | |
| 3. | Dog | < 100 (1/2 died at 50; 2/2 at 100, and higher) | -- |
| 4. | Sheep | > 200 (at 400, 1/2 died) | -- |
| 5. | Coyote | > 100 (only one animal treated) | -- |
| 6. | Swine/(Not stated) | > 50 (Only one dose used) | -- |
| 7. | Swine/(Not stated) | [No mortalities] | |

5/Gathered from (nine) unpublished and published sources (referenced by tabs in this summary report).
6/All by oral gavage, except (7), feeding five DRC-1339-poisoned starlings/day for 20 days.

1. Rat Study (Tab 2585) - All 10 animals dosed at 2500 mg/kg died within 1 (females) to 2 (males) days after treatment. Three females (but no males) were found dead 1 day after dosage at 1250 mg/kg. Depressed behavior was observed in surviving mid-dose animals, but no adverse clinical effects at lower doses. Autopsied females appeared to present normal findings; males were not autopsied (no explanation given).

2. Mouse Studies (Tabs 5142 and 12495) - DRC-1339 was lethal to all house mice (Mus musculus) treated at 1260 mg/kg and higher, as well as to all three males (but only one female) at 1000 mg/kg; no animals treated at lower doses (500, 800 mg/kg) died. In tests with field mice (Peromyscus), the ALD was calculated to be > 1600 mg/kg DRC-1339 (however, no other details were provided in the publication).

4. Dog Study (Tab 2388) - All dogs receiving 100 mg/kg DRC-1339 and higher died within 1 to 3 days after dosing, but only one of the two treated at 50 mg/kg.

6/7. Swine Studies (Tab 11220) - No animals directly gavaged once with DRC-1399 at 50 mg/kg died, and no adverse clinical or histopathological effects of treatment were reported.

None of the pigs fed poisoned birds died, nor did any exhibit any external clinical effects.

F. TB Evaluation - The required rat study is judged CORE-SUPPLEMENTARY, based upon insufficient information, in accordance with the data requirements of current FIFRA Test Guidelines. However, sufficient data were provided to designate the test material as no worse than Toxicity Category III for labeling purposes.



7

Reviewed By: Irving Mauer, Ph.D., Geneticist
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1-8-90

1/13/90

DATA EVALUATION REPORT

007683

I. SUMMARY

MRID No.: 41267206
ID No.: 56228-10
RD Record No.: 254,073
Caswell No.: 216A
Project No.: 0-0177

Study Type: (81-2) Acute dermal toxicity ($LD_{50}$) - Rabbit

Chemical: DRC-1339 [3-chloro-4-methylbenzeneamine hydrochloride]

Synonyms: Starlicide®; 3-chloro-p-toluidine HCl (CPTH)

Sponsor: USDA (APHIS)
Hyattsville, MD

Testing Facility: Denver Wildlife Research Center (USDA, S&T)
Denver, CO

Title of Report: Acute Dermal Toxicity to Rabbits for the Chemical, 3-Chloro-4-Methylbenzeneamine Hydrochloride (Compound DRC-1339; CPTH).

Author: C. Edward Knittle, citing data from an unpublished report: "Anonymous (1964). CL47,676 Avicide: Rabbit dermal." (USFWS, Wildlife Res. Ctr., Denver, CO), at Tab 2584 of the submission.

Study No.: (Special Report No. 7)

Date of Issue: September 1989

TB Conclusions:

The dermal $LD_{50}$ in rabbits for the DRC-1339 sample tested was calculated at 2680 mg/kg (males only tested).

Classification (Core-Grade):

SUPPLEMENTARY, since only summary tabulated results were submitted, i.e., reporting is incomplete according to current FIFRA Test Guidelines.

II. DETAILED REVIEW

A. Test Material - CL 47,676 Avicide [Not fully described in this submission]

Description: "Paste"
Batch (Lot): [Stated as "Sample No. 64-121/64-210"]
Purity (%): [Not stated]
Solvent: $H_2O$

B. Test Organism - Lagomorph

Species: Rabbit
Strain: (Not stated specifically for this acute $LD_{50}$ study)
Weights - Males (only), approximately 6.2 kg
Source: (Not stated)

C. Study Design (Protocol) - This study was designed to assess the acute dermal toxicity potential of DRC-1339 when administered topically to (male) rabbits. No copy of the procedures employed was included in the FINAL REPORT.

A statement affirming compliance with Agency GLPs could not be provided since the study was declared not to meet FIFRA requirements (40 CFR Part 160), because it represents a summary of information gathered from published and unpublished data on file at the Denver Wildlife Research Center, all generated prior to implementation of Part 160.

D. Procedures/Methods of Analysis and Results (Tab 2584) - The entire report consists of tabulations of (raw data) results from single topical administration of the test article to groups of five males each at five dose levels, which were (presumably) observed for 21 days after treatment. Survivors and those dying-on-study (DOS) were (presumably) autopsied.

Mortalities (1 to 2 days after dosing) were recorded as follows:

| Dose mg/kg | No. of Deaths (of 5 treated) |
|---|---|
| 10,000 | 5 |
| 5000 | 4 |
| 2500 | 3 |
| 1250 | 0 |
| 650 | 0 |

From these results, the $LD_{50}$ (dermal) was calculated [method not stated!] as 2680 mg/kg (C.I. = 1730-4150 mg/kg). Moderate to severe hemorrhaging in bladder, stomach and kidney was found in animals DOS; severely depressed behavior, bloody exudates from the anogenital area, and local eschar formation were also observed in survivors given dosages of 1250 and above.

E. TB Evaluation - CORE-SUPPLEMENTARY DATA. This 1964 study as reported in the current submission is incomplete (by any standard of requirements), but at least provides a Toxicity Category for acute dermal toxicity no worse than III.

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1-5-90

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DATA EVALUATION REPORT

I. SUMMARY

MRID No.: 41267206
ID No.: 56228-10
RD Record No.: 254,073
Caswell No.: 216A
Project No.: 0-0177

Study Type: (81-5) Primary dermal and (81-4) Primary ocular irritation - Rabbit

Chemical: DRC-1339 [3-chloro-4-methylbenzeneamine hydrochloride]

Synonyms: Starlicide®; 3-chloro-p-toluidine HCL (CPTH)

Sponsor: USDA (APHIS)
Hyattsville, MD

Reporting Facility: Denver Wildlife Research Center (USDA, S&T) Denver, CO

Author: C.E. Knittle, citing data from the following: Peoples, S.A. and J. Henry (1965): Dermal Toxicity Studies using DRC-1339 (UCal/Davis); Tab 2903 of the current submission.

Study No.: (None) Tab 2903 of Special Report No. 7 from USDA, Denver, CO

Date of Issue: September 1989, summarizing the (above) Progress Report by Peoples and Henry (UCal/Davis), dated October 1, 1965.

TB Conclusions:

1. Only minimal degrees of dermal irritation were observed following application of 1% and 10% aqueous solutions of test article to the abraded or intact skin of test animals. Reported PIS (dermal) was 0.125.

2. No ocular irritation was observed 7 days following application of 0.1 mL of a 1% solution. Reported PIS (ocular) = 0.54.

Classification (Core-Grade):

CORE-SUPPLEMENTARY for both acute studies, because of incomplete procedures and reporting (according to current FIFRA Test Guidelines).

11

II. DETAILED REVIEW

A. Test Material - DRC-1339 [no other information provided]

B. Test Organism - Lagomorph

Species: Rabbit
Strain: New Zealand White [NZW]
Age: [Not stated]
Weights - Males: [Not stated]
Females: [Not stated]
Source: [Not stated]

C. Study Design (Protocol) (Tab 2903) - This study was designed to assess the primary dermal and ocular irritation potential of DRC-1339 when administered topically to NZW rabbits. The procedures were stated to follow FDA Guidelines (in force in 1965). The studies however, do not meet current EPA requirements (40 CFR Part 160), since they represent summaries of information gathered from unpublished sources, and the data were generated prior to implementation of 40 CFR Part 160.

D. Procedures/Methods of Analysis (Tab 2903)

1. Primary Dermal Irritation - Gauze sponge patches soaked with aqueous solutions of test article (1%, 10%) were applied to the dorsal and lateral abraded and intact surfaces of groups of six NZW rabbits [sex unspecified], and kept in place for 24 hours under Saran wrap and and adhesive tape. Draize criteria for edema and erythema (scales 0, 1 to 4) were evaluated at 24 and 72 hours postdose. Scores averaged over the 3-day posttreatment period were assessed; a final score of 2 or less is considered only "mildly irritating."

2. Primary Ocular Irritation - 0.1 mL of a 1% aqueous solution of DRC-1339 was instilled in one eye of nine adult NZW rabbits (sex unspecified), the other eye serving as untreated control. In three of the nine treated rabbits, the eye was washed 4 seconds later with lukewarm water, in three 10 seconds later, but not washed in the remaining three. Ocular reactions were read 1, 2, 3, 4, and 7 days later.

E. Results

1. DRC-1339 was virtually without dermal toxicity in rabbits as recorded in summary tabulations for either concentration of test article (Report Tables I and II, attached here).

2. No ocular irritation (corneal opacity, iritis, conjunctivitis, chemosis or discharge) was stated to be evident up to 7 days postexposure [but no supporting data were included in this report as support].

F. TB Evaluation - TB assessment for both dermal and ocular irritation studies are SUPPLEMENTARY, due to insufficient information provided, according to current FIFRA Test Guidelines.

Attachment (Data Summaries)

TABLE I

1% DRC-1339

| Rabbit | Time of Observation | Unabraded Erythema | Unabraded Edema | Abraded Erythema | Abraded Edema |
|---|---|---|---|---|---|
| 1 | 24 hr. | 0 | 0 | 1 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 2 | 24 hr. | 0 | 0 | 1 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 3 | 24 hr. | 0 | 0 | 0 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 4 | 24 hr. | 0 | 0 | 0 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 5 | 24 hr. | 0 | 0 | 0 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 6 | 24 hr. | 0 | 0 | 0 | 1 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| Total | | 0 | 0 | 2 | 1 |

Primary Irritation Index = 0.125

TABLE II

10% DRC-1339

| Rabbit | Time of Observation | Unabraded Erythema | Unabraded Edema | Abraded Erythema | Abraded Edema |
|---|---|---|---|---|---|
| 1 | 24 hr. | 0 | 0 | 1 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 2 | 24 hr. | 0 | 0 | 1 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 3 | 24 hr. | 0 | 0 | 1 | 1 |
| | 72 hr. | 0 | 0 | 1 | 0 |
| 4 | 24 hr. | 0 | 0 | 0 | 0 |
| | 72 hr. | 0 | 0 | 0 | 0 |
| 5 | 24 hr. | 0 | 0 | 1 | 1 |
| | 72 hr. | 0 | 0 | 1 | 0 |
| 6 | 24 hr. | 0 | 0 | 1 | 2 |
| | 72 hr. | 0 | 0 | 1 | 0 |
| Total | | 0 | 0 | 8 | 5 |

Primary Irritation Index = 0.54