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

008430

JUL 2 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Propanil - Reregistration Response by Propanil Task Force - Acute Toxicity Studies (Guidelines Reference Nos. 81-4, 81-5, and 81-6)

Caswell No.: 325
Record Nos.: 268522, AC660,
ID No.: 0226
Project No.: 0-2042
MRID Nos.: 413605-01, 413606-01, 413604-01

FROM: William Dykstra, Reviewer William Dykstra 11/16/90
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

TO: Terri Stowe, PM Team 74
Reregistration Branch
Special Review and Reregistration Division (H7508C)

THRU: Roger Gardner, Section Head 6/10/91 (for RG)
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

6/14/91

Requested Action

Review acute toxicology studies submitted by the Propanil Task Force in support of reregistration of propanil.

Conclusion and Recommendations

The submitted studies are acceptable as core-guideline data.

1 of 2

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The results show that propanil is a moderate eye irritant (Toxicity Category II), a very slight skin irritant (Toxicity Category IV) and is <u>not</u> a dermal sensitizer in guinea pigs.

Reviews of each of these studies are attached.

Attachments

Reviewed By: William Dykstra William Dykstra 11/16/90
Section I, Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Roger Gardner, Section Head for Concurrence 6/14/91
Section I, Toxicology Branch I - IRS (H7509C) (for RG)

DATA EVALUATION REPORT 008430

Study Type: Primary Eye Irritation - 81-4 TOX Chem No.: 325

Accession Number: N/A MRID No.: 413605-01

Test Material: Propanil, Batch No. 01, 100% Purity

Study Number: Project No. WIL-141004

Sponsor: Propanil Task Force

Testing Facility: Wil Research Labs
Ashland, OH

Title of Report: Primary Eye Irritation Study in Albino Rabbits with Propanil.

Author: Dennis J. Naas

Report Issued: September 5, 1989

Conclusions:

100 mg of finely ground test material was instilled into the right eye of each of six female New Zealand White (NZW) rabbits. Draize scores were made at 1, 24, 48, and 72 hours and 4, 7, and 14 days. Conjunctivitis occurred in 6/6 which cleared by day 14. Iritis was present in 6/6 which cleared by day 14. Corneal opacity occurred in 3/6 which cleared by 4 days. Average maximum Draize score of 23.8 at 24 hours. Toxicity Category II.

Classification: Core-Guideline

Special Review Criteria (40 CFR 154.7): N/A

Review:

Primary Eye Irritation Study in Albino Rabbits with Propanil (WIL Project No. WIL-141004; September 5, 1989; MRID No. 413605-01).

Test Material - Propanil, assumed 100% purity; Batch No. 01; Supplied by Propanil Task Force. A

Animals - NZW rabbits, six females, young adult (2127 to 3043 g bwt), individually housed, Purina Certified Rabbit Chow #5322 and tap water ad libitum.

Methods - 100 mg of finely ground test material was instilled into the conjunctival sac of the right eye of each of six female rabbits. The eyelids were closed for 1 second. The eyes remained unwashed. The left eye of each animal served as a control. Observations were made at 1, 24, 48, and 72 hours and at 4, 7, and 14 days. In addition, both eyes of all rabbits were further examined at 72 hours and 7 and 14 days with sodium fluorescein and ultraviolet light.

Results - There were no mortalities. Body weight was essentially unchanged during the study period. The left eyes of all rabbits were free of irritation.

All right eyes had conjunctivitis which cleared in 7 days for 3/6 and by day 14 in the remaining 3/6. Iritis was present in 3/6 eyes which cleared by 48 and 72 hours and day 14. Corneal opacity was present in 3/6 eyes which cleared by 72 hours, 4 days, and 72 hours in the three rabbits. Average maximum Draize score at 24 hours was 23.8; Toxicity Category II, classification is considered appropriate.

Addendum - A Quality Assurance Statement was signed on August 5, 1989 by Deborah L. Little, Supervisor of Quality Assurance.

A table of primary eye irritation scores provided by the registrant in the report is shown below.

Table 1. Primary Eye Irritation Study In Albino Rabbits With Propanil

Project No: WIL-141004
Sponsor: Propanil Task Force

Individual Ocular Irritation Scores

Group: 100 mg/Right Eye, Unwashed			Examination Intervals						
Animal	Sex	Tissue	1 H	24 H	48 H	72 H*	4 D	7 D*	14 D*
8483	F	Cornea (O-A)	0 0	0 0	0 0	0 0	0 0	0 0	
		Iris	0	0	0	0	0	0	
		Conjunctiva (R-C-D)	2 2 1	2 1 0	1 1 0	1 0 0	1 0 0	0 0 0	
8490	F	Cornea (O-A)	0 0	2 3	2 1	0 0	0 0	0 0	0 0
		Iris	0	1	1	0	0	0	0
		Conjunctiva (R-C-D)	2 3 2	3 3 2	2 2 0	2 1 0	1 0 0	1 1 0	0 0 0
8497	F	Cornea (O-A)	2 3	2 3	2 2	1 2	0 0	0 0	0 0
		Iris	1	1	0	0	0	0	0
		Conjunctiva (R-C-D)	2 2 2	2 2 2	1 1 0	1 1 0	1 0 0	1 0 0	0 0 0
8499	F	Cornea (O-A)	0 0	0 0	0 0	0 0	0 0	0 0	
		Iris	0	0	0	0	0	0	
		Conjunctiva (R-C-D)	2 2 2	2 1 0	2 1 0	1 0 0	1 0 0	0 0 0	
8505	F	Cornea (O-A)	0 0	0 0	0 0	0 0	0 0	0 0	
		Iris	0	0	0	0	0	0	
		Conjunctiva (R-C-D)	2 2 2	2 1 0	2 0 0	1 0 0	0 0 0	0 0 0	
8507	F	Cornea (O-A)	1 1	2 1	1 1	0 0	0 0	0 0	0 0
		Iris	1	1	1	1	1	1	0
		Conjunctiva (R-C-D)	2 3 2	3 2 1	2 1 0	2 0 0	1 0 0	0 0 0	0 0 0
Total			119.	143.	77.	35.	17.	11.	0.
Mean			19.8	23.8	12.8	5.8	2.8	1.8	0.0

* = Fluorescein Solution Applied; O = Opacity; A = Area; R = Redness; C = Chemosis; D = Discharge; H = Hours; and D = Days.

Classification: Core-Guideline

Reviewed By: William Dykstra William Dykstra 11/28/90
Section I, Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Roger Gardner, Section Head
Section I, Toxicology Branch I - IRS (H7509C)

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DATA EVALUATION REPORT

Study Type: Primary Dermal Irritation - 81-5 TOX Chem No.: 325

Accession Number: N/A MRID No.: 413606-01

Test Material: Propanil, 100% Purity, Batch 01

Synonyms: None

Study Number: Project No. WIL-141003

Sponsor: Propanil Task Force

Testing Facility: Wil Research Labs
Ashland, OH

Title of Report: Primary Dermal Irritation Study in Albino Rabbits with Propanil.

Author: Dennis J. Naas

Report Issued: September 5, 1989

Conclusions:

0.5 g of finely ground, moistened, test material was applied under occlusion for 4 hours to shaved, intact skin of six rabbits (4F and 2M). Scoring according to Draize at 4-5, 24, 48, and 72 hours showed very slight erythema in four rabbits and very slight edema in one rabbit at 4-5 hours which cleared by 24 hours. P.I.S. = 0.2/4.0; Toxicity Category IV.

Classification: Core-Guideline

Special Review Criteria (40 CFR 154.7): N/A

Review:

Primary Dermal Irritation Study in Albino Rabbits with Propanil (WIL Project No. WIL-141003; September 5, 1989; MRID No. 413606-01).

Test Material - Propanil, 100% purity; Batch No. 01; provided by Propanil Task Force.

Animals - New Zealand White rabbits - two males and four females, 2463 to 3086 g bwt at study initiation; individually housed; tap water and Purina Rabbit Chow #5322 ad libitum.

Methods - 0.5 g of finely ground test material, moistened, was applied directly to the shaved, intact skin of each of six rabbits at one intact site per rabbit. The test material was occluded and the animals wore plastic restraint collars. The test material remained in contact with the rabbit's skin for 4 hours. At the end of 4 hours, the collars and bandages were removed and the sites wiped with wet disposable paper towels. Sites were scored according to Draize for erythema, edema, and any other dermal findings at 4-5, 24, 48, and 72 hours after dosing.

Results - There were very slight erythema in four rabbits and very slight edema on one rabbit at the initial 4-5 hour observation period which had disappeared by 24 hours. Primary irritation index was 0.2/4.0. Toxicity Category IV.

There were no mortalities and body weight was not remarkably changed during the study period.

Addendum - A Quality Assurance Unit statement was signed on September 5, 1989 by Deborah L. Little, Supervisor of Quality Assurance.

The following table from the report shows individual results.

Table 1. Primary Dermal Irritation in Albino Rabbits

Project No.: WIL-141003
Submission Propanil Task Force

Individual Dermal Scores

			INTACT					INTACT			
			Erythema		Edema			Erythema		Edema	
Animal	Sex	Site	4-5 H	24 H	4-5 H	24 H	Site	48 H	72 H	48 H	72 H
8401	M	A	1	0	0	0	A	0	0	0	0
8403	M	A	1	0	0	0	A	0	0	0	0
8406	F	A	0	0	0	0	A	0	0	0	0
8408	F	A	1	0	0	0	A	0	0	0	0
8412	F	A	1	0	1	0	A	0	0	0	0
8422	F	A	0	0	0	0	A	0	0	0	0
		Total	4	0	1	0	Total	0	0	0	0

PII Calculated Using Test Periods 4-5 H, 24 H, 48 H, 72 H.
Primary Irritation Index (PII) = (4 + 0 + 0 + 0 / 24) + (1 + 0 + 0 + 0 / 24)
(PII) = 4 / 24) + (1 / 24)
(PII) = 0.2 + 0.0
(PII) = 0.2 = Slightly Irritating

H = Hours; M = Male; and F = Female.

Classification: Core-Guideline

Reviewed By: William Dykstra 11/16/90
Section I, Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Roger Gardner, Section Head
Section I, Toxicology Branch I - IRS (H7509C)

008130

DATA EVALUATION REPORT

Study Type: Dermal Sensitization - 81-6 TOX Chem No.: 325

Accession Number: N/A MRID No.: 413604-01

Test Material: Propanil, 100% Purity, Batch 01

Synonyms: None

Study Number: Project No. WIL-141005

Sponsor: Propanil Task Force

Testing Facility: Wil Research Labs
Ashland, OH

Title of Report: Skin Sensitization Study in Albino Guinea Pigs with Propanil.

Author: Dennis J. Naas

Report Issued: September 5, 1989

Conclusions:

Propanil was tested in a modified Buehler method for topical skin sensitization in Hartley Albino guinea pigs. There was a primary irritation phase to select the concentrations of propanil solution for the induction (25% propanil solution) and challenge phases (2.5% propanil solution). There were nine induction doses over a 3-week period. After 14 days from the last induction dose, challenge doses to the propanil group, a naive control group, and a positive control group, DNCB, were performed. Propanil was not a skin sensitizer in comparison to the naive controls. The positive control group produced skin sensitization in all animals.

Classification: Core-Guideline

Special Review Criteria (40 CFR 154.7): N/A

Review:

Skin Sensitization Study in Albino Guinea Pigs with Propanil (WIL Project No. WIL-141005; September 5, 1989; MRID No. 413604-01).

Test Material - Propanil, 100% purity; Batch No. 01; provided by Propanil Task Force; positive control was 0.1 percent w/v dinitrochlorobenzene in 80 percent ethanol.

Animals - Hartley Albino guinea pigs, 12 males and 12 females, Murphy Breeding Laboratories, Inc., Plainfield, IN, 314 to 399 g, young adults, individually caged, Purina Guinea Pig Chow #5025 and tap water ad libitum.

Experimental Design:

1. Primary Irritation Phase - Test material was prepared for dosing as w/v solutions in acetone at concentrations of 1.0, 2.5, 5, 10, and 25 percent.

2. Induction - The 25 percent w/v solution of propanil in acetone was chosen for induction. The positive control was 0.1 percent w/v solution in 80 percent ethanol with dinitrochlorobenzene.

3. Challenge Phase - Test material was 2.5 percent w/v solution in acetone. Positive control was 0.1 percent dinitrochlorobenzene.

4. Test Material Administration - Direct topical occluded application to shaved, intact skin. This route of administration is the modified Buehler method.

   a. Primary Irritation Phase - 0.4 mL/site. There were three test sites per guinea pig. The period of exposure was 6 hours.

   b. Induction Phase - The 25 percent w/v prepared test material and positive control materials were applied occluded at 0.4 mL/site. Induction doses were applied to the same site on the left flank of all test and positive control group animals. Test and positive control group animals each received nine induction doses spaced 2 or 3 days apart over a period of 3 weeks. All induction exposures were 6 hours, after which bandages were removed and the sites washed with wet disposable paper towels.

      All naive control animals remained untreated during the induction phase.

c. Challenge Phase - 14 days after the last induction, the test and naive control group animals were dosed with 0.4 mL/site of a 2.5 percent w/v solution of propanil in acetone on the right flank. Positive control animals were dosed with a 0.1% w/v dinitrochlorobenzene in 80 percent ethanol at 0.4 mL/site on the right flank.

Dermal Observations - All sites were examined and graded in accordance with the score scale at 24 and 48 hours (score scale 0, ±, 1, 2, 3, 4, = no reaction, slight patchy erythema, slight confluent or moderate patchy erythema, moderate erythema, severe erythema (with or without edema).

Results:

1. Mortality - Naive control group I female 04001171 was sacrificed on study day 7. This study animal was replaced. No other deaths occurred.

2. Body Weight - No remarkable weight changes.

3. Dermal Observations

a. Primary Irritation Phase - 25 percent propanil acetone solution was lowest concentration that induced consistent, very slight to slight reactions.

The 25 percent propanil solution was the highest concentration that produced no irritation and was selected for challenge dose.

b. Challenge Phase - One test group animal (propanil) and two naive control animals produced slightly patchy erythema (scores of ±) observed at 24 hours. All other test sites in the propanil test group or naive control were negative. In the positive control group, grade 2 or 3 persisted through 48 hours in all animals. The table below shows the results.

(Report Table 8)

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"Table 8. Skin Sensitization Study in Albino Guinea Pigs with Propanil

Project No.: WIL-141005
Sponsor: Propanil Task Force

Incidence of Dermal Responses at Challenge

Group	Material	Interval	Dermal Scores 0	±	1	2	3	Number of Animals	Irritation Severity Index
Test	2.5% w/v Propanil in acetone	24 H	11	1	0	0	0	12	0.04
		48 H	12	0	0	0	0	12	0.0
Naive Control-I	2.5% w/v Propanil in acetone	24 H	4	2	0	0	0	6	0.1
		48 H	6	0	0	0	0	6	0.0
Positive Control	0.1% DNCB	24 H	0	0	0	1	5	6	2.8
		48 H	0	0	0	5	1	6	2.2

H = Hours.
DNCB = Dinitrochlorobenzene.

Conclusion - Propanil is not a skin sensitizer in this experimental design. The positive control, dinitrochlorobenzene, produced positive skin sensitivity results.

Addendum - A Quality Assurance Unit statement was signed on September 5, 1989 by Deborah L. Little, Supervisor of Quality Assurance.

Classification: Core-Guideline