9/28/73

Ocular Irritation and Dermal Screening Tests of ID 101852 (Tordon 22K Weed Killer, Reg. No. 464-323).

Objective

The purpose of this study was to determine the ocular irritation potential of Tordon 22K. The study was initiated because of a reported human accident resulting in substantial, permanent ocular damage subsequent to contact with this material. (Details of the accident have not been made available to us.) A dermal screening test was run as an adjunct to the ocular study.

Material

Tordon 22K Weed Killer, with Reg. No. 464-323, is a product of the Dow Chemical Co. The active ingredient listed on the label is Picloram as the potassium salt (4-amino-3,5,6 trichloropicolinic acid) - 24.9%. The product had been routinely collected as ID 101852, a clear, amber liquid in a one-half gallon plastic container with "#10561" stamped on the bottom. This sample was utilized in the animal tests reported herein.

Methods

Ocular Irritation Test

Six healthy adult albino rabbits were selected for this test after passing a physical examination including close inspection of the eyes. Each animal received 0.1 ml of the product placed in the conjunctival sac formed by cupping the lower lid of the left eye; this eye was not further treated. The right eye was not treated and served as a control. The animals were closely watched for any signs of immediate reaction to the treatment and were observed daily (five times weekly) until all effects had disappeared. Grading of the ocular responses was made according to the guidelines of Draize*.

Dermal Screening Test

Two healthy adult albino rabbits were used for this test. A small area next to the nuchal region was clipped free of fur. A cross-hatch pattern, comprised of two sets of parallel nonbleeding abrasions made at ninety degrees to each other, was formed in the proximal portion of the clipped area. Each site, intact and abraded, was treated with 0.5 ml of the product and covered with a 7.6 x 11.4 cm sterile adhesive bandage. After 24 hours the bandages were removed and the treated sites were graded then and again at 48 and 72 hrs and seven days postdose.

---

*Appraisal of the safety of chemicals in foods, drugs and cosmetics. 1959, Assoc. of Food and Drug Officials of the U.S.A.

1/9 80

Results and Summaries

Ocular Irritation Test

Results of the ocular test are summarized in Table 1. Control eyes remained normal in appearance throughout the study.

Signs indicative of strong pain were not seen in any of the animals upon application of the sample; yet shortly after dosing each animal showed some degree of conjunctivitis and kept the treated eye closed.

Mild iritis was noted in three of the animals at 24 hrs and all continued to show conjunctivitis. Within 48 hrs all iridal irritation had disappeared and two animals now were free of any conjunctival effects and the membranes of the other animals had improved. Mild conjunctivitis persisted through 72 hrs in three animals but had disappeared by the fourth day postdose. Thus, all treated eyes appeared normal within 96 hrs and no further observations were made.

In summary, Tordon 22K applied to the eye induced prompt conjunctivitis in all animals which persisted at a mild level through the third day and mild iritis which cleared by the second day.

Dermal Screening Test

Averaged results of the dermal test are presented on report forms for this procedure.

Both of the animals showed erythema and edema along the abrasions at 24 hrs but no evidence of an effect was noted in the intact sites. Erythema of slight degree was still present in the abraded site of one animal at 48 hrs but this minimal effect had disappeared by the next day.

Thus, to summarize, Tordon 22K applied to the skin affected only abraded areas, inducing mild erythema and edema initially which disappeared by 72 hrs postdose.

W R. Teeters
W.R. Teeters, Ph.D.
Supervisory Pharmacologist

Enclosures:

Table 1.
Dermal irritation reports (2)

cc: W. Waldrop, Accident Investion
Sec., Div. of Operations
D.T. von Sumpter, TSD

2

281

Table 1. Ocular irritation scores of rabbits following treatment with **ID 101852, Tordon 22K Weed Killer.**

INDIVIDUAL SCORES *

Interval	24 hrs						48 hrs						72 hrs						96 hrs						7th day						14th day					
Rabbit No.	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
Cornea																																				
a) Opacity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0																		
b) Area	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0																		
Iris																																				
a) Injury	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0																		
Conjunctiva																																				
a) Redness	3	3	3	3	3	1	0	2	1	2	2	0	0	1	0	2	2	0																		
b) Chemosis	1	1	1	1	1	0	0	0	0	1	1	0	0	0	0	1	1	0																		
c) Discharge	3	2	2	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0																		

***All scores left blank were zero.**

Weighted Average Total Scores

	24 hrs	48 hrs	72 hrs	96 hrs	7th day	14th day
Cornea (axbx5) Maximum = 80	0	0	0	0	0	0
Iris (ax5) Maximum = 10	2.5	0	0	0	0	0
Conjunctiva (a+b+c)x2 Maximum = 20	10.3	3	1.7	0	0	0

PHARMACOLOGY LABORATORY - DERMAL IRRITATION

ID Sample No. 101852 Reg. No. 464-323 Lot No. -- Date test ended: 9/18/73

Product Name & Company: TORDON 22K Weed Killer; The Dow Chemical Co., Midland, Mich.

Form/Type: EC[X] WP[ ] PS[ ] AERO[ ] DUST[ ] OTHER[ ]

Ingredients:

Picloram as the potassium salt (4-amino-3,5,6 trichloropicolinic acid) 24.9%

Inert ingredients: 75.1%

SKIN: Examined and treated according to skin irritant test procedure.

Dose: 0.5 ml ____ mg

Number of Animals 2 ANIMAL: Rat[ ] Rabbit[X] G.P.[ ]

RESULTS

Time	Erythema & Eschar Formation	Edema Formation
24 hrs	2	3
48 hrs	0	0
72 hrs	0	0
7 days	0	0
14 days		

(Grading key on reverse)

Remarks:

Each animal was tested in two areas, one abraded, one intact. Above results are the averages of the abraded areas of both animals.

Tested by: A. Arce D.L. Maxey

(Signature) Pharmacologist in Charge W.R. Teeters

W.R. Teeters

PR Form 7-3a Rev. 5/24:8/5/69;5/3/71

4 287

EVALUATION OF SKIN REACTIONS: GRADING CHART

(1) Erythema and eschar formation

NO erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Total possible erythema score	4

(2) Edema formation

NO edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Total possible edema score	4

PHARMACOLOGY LABORATORY - DERMAL IRRITATION

ID Sample No. 101852 Reg. No. 464-323 Lot No. -- Date test ended: 9/18/3

Product Name & Company: TORDON 22K WEED KILLER; The Dow Chemical Co., Midland, Mich.

Form/Type: EC[X] WP[] PS[] AERO[] DUST[] OTHER[]

Ingredients:

Picloram as the potassium salt (4-amino-3,5,6 trichloropicolinic acid) 24.9%

Inert ingredients: 75.1%

SKIN: Examined and treated according to skin irritant test procedure.

Dose: 0.5 ml ____ mg

Number of Animals 2 ANIMAL: Rat[] Rabbit[X] G.P.[]

RESULTS

Time	Erythema & Eschar Formation	Edema Formation
24 hrs	0	0
48 hrs	0	0
72 hrs	0	0
7 days	0	0
14 days		

(Grading key on reverse)

Remarks:

Each animal was treated in two areas, one abraded, one intact. Above results are the averages from the intact areas of both animals.

Tested by: A. Arce D.L. Maxey

(Signature) Pharmacologist in Charge W.R. Teeters

PR Form 7-3a Rev. 5/24:8/5/69;5/3/71 5/3/71

6 285

EVALUATION OF SKIN REACTIONS: GRADING CHART

(1) Erythema and eschar formation

NO erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Total possible erythema score	4

(2) Edema formation

NO edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Total possible edema score	4

PHARMACOLOGY LABORATORY TOXICITY REPORT - SCREENING

ID No. 101852 Code(s): -- Reg.No. 464-323 Date: 9/11/73 (test ended)

Product Name & Company: TORDON 22K Weed Killer;
The Dow Chemical Co., Midland, Mich.

Form/Type: [X]EC [ ]WP [ ]PS [ ]Aero [ ]Dust [ ]Other_____

Ingredients:

Picloram as the potassium salt (4-amino-3,5,6 trichloropicolinic acid)	24.9%
Inert ingredients:	75.1%

TEST:
Type: ACUTE, SCREENING

Route: Oral[X] Dermal[ ] Other[ ]

Animal: Rat[X] Rabbit[ ] G.P.[ ] Mouse[ ]

DATA: (1st no. = *no. animals dead;* 2nd no. = *no. animals treated;* 3rd no. = *day dead, posttreatment.*
EXAMPLE: 1/2/1 means *1 animal dead of 2 treated, on day 1.)*

Dose (ml /kg)	♂	♀	Total	Dilution
2.5	0/2/7	0/2/7	0/4/7	None.
5.0	0/2/7	1/2/1	1/4/7	
10.0	0/2/7	2/2/0	2/4/7	

SYMPTOMS: General to profound depression; severe convulsion at high dose.

RESULTS: FORMULATION TOXICITY

Lab ALD, Screen: 10 gm/kg Major ingredient(s) LD_{50}_____/kg

Screen Category: III Label Category (Label not available)

[ ]LABELING DEFECTIVE; REQUIRED LABELING (CATEGORY)_____.

Tested by:
H.O. Williamson W.E. McDuffie

(Signature) Pharmacologist in Ch
W.R. Teeters

EPA-TSD Form 7-3 Rev. 1/10/73 *Formerly PR Form 7-3 Rev. 6-*

8 287

HISTORY OF OFFICIAL SAMPLE

1. SAMPLE NUMBER: ID 101852

2. PRODUCT: XTRX Tordon 22K Weed Killer

3. Laboratory	PHARMACOLOGY LABORATORY
4. Date received	31 AUG 1973
5. Received by	Haw
6. Received from	Denver
7. Sent via	U.S. Mail
8. Sample Condition	O.K
9. Condition of seals	intact
10. Sealed by	H & J
11. Date Sealed	5-31-73
12. Pieces received	1
13. Place stored	B-7
14. Assigned by	WET
15. Assigned to	Haw
16. Delivered by	Wmc D
17. Date delivered	31 AUG 1973
18. Number subs received	1
19. Subs analyzed	1
20. Date sealed	31 AUG 1973 31 AUG 1973
21. Sealed by	Haw
22. Place stored	PHARMACOLOGY LABORATORY
23. Date jacket sent out	28 SEP 1973

24. REMARKS

FOR USE BY ID RECORDS

25. REGISTRATION NUMBER: 464-323

PR FORM 1-136
MAY 1967

EXISTING STOCK OF PR FORM 1-136, APR 1962, WILL BE USED UNTIL EXHAUSTED

USDA-ARS

9 28