BB-691
10-25-78
TOX-669

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 000669 ©

DATE: October 23, 1978

SUBJECT: Review of Acute Toxicity Studies submitted in request for permanent tolerances for endothall. Caswell [redacted], EPA Registration#4581-204

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FROM: William Dykstra, Ph.D
TOX/HED TS-769

10/25/78 WHD

TO: Henry M. Jacoby
Product Manager#24

Pesticide Petition: 1F1105

Food Additive Petition: 2H5016

Petitioner: Pennwalt Corporation

Recommendations:

1. The Acute toxicity studies can be added to the petitioner's file on endothall formulations.

2. Some studies are by IBT and need to be validated.

I. Review of Submitted Studies.

Section VII. Human Safety.

Exhibit 136. Letter and data A.R. Latven to Obren Keckemet - Nov. 18, 1975.

Letter summarizes primary eye irritation and dermal toxicity of seven (7) products submitted for evaluation. Washing the eye within 30 sec. after instillation decreased the irritant reaction significantly. This applies primarily to the incidence of corneal opacity since washing had little effect upon conjunctival inflammation or iridal congestion. That the rabbit may be hypersensitive to endothall is a distinct possibility. The rat has been shown to be much more resistant. Thus the question remains open whether the rat or the rabbit reflects man's sensitivity to this product. The lack of toxicological accidents under field conditions suggest that the rabbit may very well be hypersensitive.

1. Endothall Technical (N.B. 58-196-2) (Pharmacology Research, Inc., 11.18/75), white powder; Method: 0.1 gm was placed in the conjunctival sac of one eye of each of six albino rabbits. The treated eye of three of these animals was washed following with flowing water initiated 20 to 30 seconds after instillation and continued for one minute.

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Results: Unwashed: Conjunctival inflammation (score 2) with iridal congestion (score < 1) developed promptly and corneal opacification (score 2) appeared with 2 hours. Each of the three rabbits died overnight.

Washed: The reaction in two of the rabbits was confined to conjunctival inflammation and iridal congestion with full recovery within 5 days. In the third animal the reaction developed in greater intensity, included corneal opacification, and persisted for at least 7 days.

Classification: Core-Minimum Data TOX Category I: DANGER

b. Acute Dermal Toxicity in Rabbits; Method: A single dose of 200 mg/kg was spread upon the wetted skin of the fur-clipped trunk of each of six albino rabbits, covered with a wet two-ply layer of gauze, and overcovered with an impervious sleeve. Intended skin contact time was 24 hours.

Results: Each of the six rabbits died overnight.

Classification : Supplementary Data TOX Category I: DANGER

(1) LD_{50} was not determined.

(2) Accelerate (N.B. 58-196-3) a clear yellow liquid. a. Eye Irritation Study. Method: 0.1 ml was placed in the conjunctival sac of the left eye of six albino rabbits. In three of these animals the right eye was also treated but was washed with flowing water 20 to 30 sec. After instillation and continued for a period of one minute.

Results: Unwashed: conjunctival inflammation with iridal congestion developed promptly and corneal clouding appeared 24 to 72 hours after instillation. These effects persisted for at least 7 days in all but one animal; the latter showed no corneal effects and recovered completely within 5 days.

Washed: The reaction was confined to conjunctival inflammation with full recovery within 5 days.

Classification: Core-Minimum Data TOX Category I: DANGER

(3) Aquathol K (N.B. 58-196-4) a clear, ambers liquid. density = 1.270 gm/ml

a. Eye Irritancy in Rabbits. Method: 0.1 ml was placed in the conjunctival sac of the left eye of each of six albino rabbits. In three of these animals the right eye was also treated but was washed with flowing water initiated 20 to 30 sec. after instillation and continued for a period of one minute.

Results: Unwashed: conjunctival inflammation with iridal congestion developed promptly and corneal clouding appeared four to six days after instillation. These effects persisted for at least 7 days following treatment.

Washed: The reaction was confined to conjunctival inflammation and iridal congestion with full recovery within 5 days.

Classification: Core-Minimum Data TOX Category I: DANGER

b. Acute Dermal Toxicity in Rabbits.

Method: A single dose of 200 mg/kg (0.1 ml of a 20% w/v aqueous dilution) was spread upon the skin of the fur-clipped trunk of each of six albino rabbits and covered with an impervious sleeve. After a skin-contact period of 24 hours, the sleeve was removed from the surviving animal and the treated area was cleansed with tepid water, the animals were then observed for 7 days.

Results: five of the six rabbits died overnight.

The sole survivor lost body weight for three days because of anorexia; However, this was recovered within 7 days after treatment.

TOX Category I: DANGER Classification Supplementary Data

(1) The LD_{50} was not determined.

(3.) Herbicide 283 (N.B. 58-196-5) a clear, amber liquid density = 1.04 gm/ml

a. Eye Irritancy in Rabbits.

Method: 0.1 ml was placed in the conjunctival sac of one eye of each of six albino rabbits. The treated eye of three of these animals was washed with flowing water initiated 20 to 30 seconds after instillation and continued for one minute.

Results: Unwashed: Conjunctival inflammation, iridal congestion, and corneal opacification developed promptly. These effects persisted for at least 7 days.

Washed: The reaction in two of the rabbits was confined to conjunctival inflammation and iridal congestion with full recovery within 6 days. In the third animal the reaction developed in greater intensity, included corneal opacification, and persisted for at least 7 days.

Classification: Core-Minimum Data TOX Category I: DANGER

b. Acute Dermal Toxicity in Rabbits.

Method: A single dose of 200 mg/kg (1.0 ml/kg of a 20% w/v aqueous dilution) was spread upon the skin of the fur-clipped trunk of each of six albino rabbits and covered with an impervious sleeve. The intended time of skin contact was 24 hours.

Results: Each of the six rabbits died over night. Three additional animals exposed to the same dose for one hour (rather than 24 hours) showed no ill effects.

Classification: Supplementary Data TOX Category I: DANGER

(1) LD_{50} was not determined.

(4) Hydrothol 47 (N.B. 58-196-6) a clear, amber liquid; Density - 0.98 gm/ml.

a. Acute Dermal Toxicity in Rabbits.

Method: A single dose of 200 mg/kg (1.0 ml/kg of a 20% w/v aqueous dilution) was spread upon the skin of the fur-clipped trunk of each of six albino rabbits and covered with an impervious sleeve. After a skin-contact period of 24 hours, the sleeves were removed from the surviving animals and the treated areas were cleansed with tepid water; These animals were then observed for 7 days.

Results: five of the six rabbits died within 4 days. None of these animals ingested any food or water after treatment. TOX Category I: DANGER. The sole survivor lost body weight for three days because of anorexia; However, this was recovered within 7 days after treatment.

Classification: Supplementary Data

(1) LD_{50} was not determined.

(5) Aquathol Granular (N.B. 58-196-7) A brown-gray, granular solid.

a. Eye Irritancy in Rabbits.

Method: The sample was ground to a fine powder for use in this study. 0.1 gm was placed in the conjunctival sac of the left eye of each of six albino rabbits. In three of these animals the right eye was also treated but was washed with flowing water initiated 20 to 30 seconds after instillation and continued for a period of one minute.

Results: Unwashed: Conjunctival inflammation with iridal congestion developed promptly whereas corneal opacification appeared slowly and was complete within 5 days. These effects persisted for at least 7 days after treatment.

Washed: The reaction was confined to conjunctival inflammation with full recovery within 5 days.

Classification: Core-Minimum Data TOX Category I: DANGER

(6.) Hydrothol 47 Granular (N.B. 58-196-8) a brown-gray, granular solid.

a. Eye Irritancy in Rabbits.

Method: The sample was ground into a fine powder for use in this study. 0.1 gm was placed in the conjunctival sac of the left eye of six albino rabbits. In three of these animals the right eye was also treated but was washed with flowing water initiated 20 to 30 seconds after instillation and continued for a period of one minute.

Results: Unwashed: Conjunctival inflammation with iridal congestion developed promptly and corneal opacification appeared within 24 hours. These effects persisted for at least 7 days after treatment.

Washed: The reaction was confined to conjunctival inflammation with full recovery within four days.

Classification: Core-Minimum Data TOX Category I: DANGER

b. Acute Dermal Toxicity in Rabbits.

Method: Doses of the granular sample were spread upon the wetted skin of the fur-clipped trunks of albino rabbits, covered with a two-ply layer of gauze, and overcovered with an impervious sleeve. After a skin-contact period of 24 hours, the sleeves were removed and the treated areas cleansed with tepid water. The animals were observed for 7 days. Three rabbits were treated with 2000 mg/kg and six rabbits were treated with 200 mg/kg.

Results: 2000 mg/kg. one death. Two rabbits lost body weight.

200 mg/kg. None of the six rabbits showed any ill effects and all gained weight during post exposure period of observation. TOX Category III: CAUTION. Classification: Supplementary Data

(1) LD_{50} was not determined.

Exhibit 137. Letter and data A.R. Latven to Obren Keckemet - June 26, 1975.

Letter states that reports presenting toxicological findings with Alcoholic Ripenthol and with aqueous Riperthol show statistically simialr acute oral LD_{5C} and acute dermal LD_{50}. The oral LD_{50} is Toxicity Category III (575 mg/kg; Caution) but the Acute Dermal LD_{50} is 125 mg/kg (Toxicity Category I: Danger.) Although the rabbit is 5 times more sensitive than us the rat to these product, the matter of importance is the rapid and efficient percutaneous absorption of either liquid. This property renders the products hazardous insofar as humans are concerned.

The undiluted liquids were corrosive following contact with the eye and skin of rabbits. In summary, the principle hazards of both formulations appear to be (1) eye and skin corrosivity of the concentrate and (2) skin absorption of either the concentrate or dilutions thereof.

(A.) Ripenthol N.B. 58-196-3 (isopropyl-butanolformulation) (Pharmacology Research, Inc., 6/25/75)

Test material is an amber colored liquid; ambient density = 1.018 gm/ml.

Summary

(1) Acute Oral LD_{50} (rats) (male) = 590 mg/kg TOX CAT. III CAUTION
(2) Acute Dermal LD_{50} (rabbits) = 120 mg/kg TOX CAT. I: DANGER
(3) Eye Irritation in Rabbits: corrosive. DANGER
(4) Skin Irritation in Rabbits: necrosis. DANGER

1. Acute Oral Toxicity in Rats.

Five groups of 5 male WBS/Wistar Rats, 230 $\pm$ gm body weight, received by stomach tube an oral dose of $\angle$ 350, 350, 500, 700 and 1000 mg/kg of test material. The animals were observed for 3 days. Necropsy and body weights were determined.

Results: LD_{50} = 590 mg/kg (males)

Toxic Signs: General depression

Body Weight: Anorexia caused marked loss

Necropsy: gastric inflammation

Classification: Core-Minimum Data

TOX Category III: CAUTION

2. Acute Dermal Toxicity in Rabbits.

Aqueous dilutions of the sample were spread upon the skin of the fur-clipped trunks of albino rabbits and covered with an impervious sleeve; all doses were contained in 2.0 ml/kg. Three animals per dose level were treated at 70, 100, 140 and 200 mg/kg. After a skin-contact period of 24 hours, the sleeves were removed and the treated areas were cleansed with tepid water. Observation was for 14 days.

Results: LD_{50} = 120 mg/kg

Toxic Signs: General depression

Necropsy: Dead rabbits were in opisthotonic position.

Body Weight: Weight loss in survivors

Classification: Core-Minimum Data

TOX Category I: DANGER

3. Eye Irritancy in Rabbits.

Method: 0.1 ml of the undiluted sample was placed in the conjunctival sac of one eye of six albino rabbits. The reactions were scored periodically for one week.

Results: The cornea became totally opacified within 4 hours and the iris was seen to be congested before obscuration. A white discharge appeared within 24 hours. No signs of recovery were evident seven days after instillation.

Classification: Core-Minimum Data

TOX Category I: DANGER

4. Skin Irritancy in Rabbits.

0.5 ml of the undiluted sample was applied to one intact and one abraded skin site under standard gauze patches on opposite flanks of each of six albino rabbits. The entire fur-clipped trunk was then covered with an impervious sleeve for a skin-contact period of 24 hours.

Results: All of the rabbits died overnight as a result of percutabeous toxicity. In all case the treated sites were distinctly necrotic in appearance.

Classification: Core-Minimum Data

TOX Category I: DANGER

B. Ripenthol N.B. 58-191-2 (water only formulation) (Pharmacology Research, Inc., 6/25/75)

An amber colored liquid; ambient density = 1.027 gm/ml.

Summary

(1) Acute Oral LD_{50} = 560 mg/kg (rats, males) TOX CAT III: CAUTION
(2) Acute Dermal LD_{50} = 130 mg/kg (rabbits) TOX CAT. I: DANGER
(3) Eye Irritancy in Rabbits - corrosive. TOX CAT. I: DANGER

1. Acute Oral Toxicity in Rats.

Five groups of 5 male WBS/Wistar Rats, 230 gm body weight, received by stomach tube doses of 250, 350, 500, 700 and 1000 mg/kg of test material. Observation for 8 days.

Results: LD_{50} = 560 mg/kg (males)

Toxic Signs: General depression

Necropsy: gastric inflammation

Body Weight: marked weight loss in survivors

Classification: Core-Minimum Data

TOX Category III: CAUTION

2. Acute Dermal Toxicity in Rabbits.

Aqueous dilutions of the sample (5 to 10% w/v), were spread upon the skin of the fur-clipped trunks of three rabbits per group and covered with an impervious sleeve. Doses of 100, 140 and 200 mg/kg were applied to three groups. After a skin contact period of 24 hours, the sleeves were removed and the treated areas cleansed with tepid areas cleansed with tepid water. Observation for 14 days.

Results: LD_{50} = 130 mg/kg

Toxic Signs: General depression

Necropsy: opisthotonic position

Body Weight: weight loss in survivors

Classification: Core-Minimum Data

TOX Category I: DANGER

3. Eye Irritancy in Rabbits.

0.1 ml of the undiluted sample was placed into the conjunctival sac of one eye of each of six albino rabbits. The reactions were scored periodically for one week.

Results: The cornea became totally opacified within 4 hours and the iris was seen to be congested before obscuration. Rapidly developing edema. White discharge at 24 hours. No signs of recovery were evident seven days after instillation.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 138, (Pharmacology Research, Inc.) 8/14/75 Letter and data A.R. Latven to Obren Keckemet - August 14, 1975

Letter indicates that Dermal LD_{50} of Ripenthol in rats is 590 mg/kg which is essentially the same as oral LD_{50} (560 mg/kg). This differs greatly from the rabbit data thereby questioning the latter in any decision making process. It also dispels the notion that Ripenthol may be more toxic dermally than by oral ingestion. Rapid and efficient percutaneous absorption explains mortalities.

(1.) Ripenthol N.B. 58-191-2 (23.4%) an amber colored liquid; ambient density = 1.027 gm/ml.

Summary: Acute Dermal LD_{50} = 590 mg/kg in male rats. Applied doses were absorbed within 4 hours.

Method: Aqueous dilutions of the sample were spread upon the skin of the fur-clipped trunks of rats (male TAC/SD, 340 ± gm BW) and covered with impervious sleeves; all doses were contained in 2.0 ml/kg. Five groups of 5 rats per group received doses of 350, 500, 700, 900 and 1000 (4 hours only). After a skin-contact period of 24 hours, the sleeves were removed and the treated areas cleansed with tepid water. Surviving animals were observed until lost body weight was restored (8 to 13 days).

/Results: LD_{50} = 590 mg/kg (male rats)

100% mortality at 1000 mg/kg for 4 hours.

Toxic Signs: General depression

Body Weight: survivors lost weight for 3 days.

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 139. Letter and data A.R. Latven to Obren Keckemet. Jan. 29, 1976. (Pharmacology Research, Inc.)

Letter is a summary of submitted data.

Summary: When skin-contact time was limited to one hour, none of the four endothall products was lethal to rabbits at the 200 mg/kg dosage level.

(1.) Endothall Products, Dermal Toxicity After Limited Exposure.

Method: A single dose of 200 mg/kg (1.0 ml/kg of a 20% w/v aqueous dilution) was spread upon the skin of the fur-clipped trunks of albino rabbits and covered with an impervious sleeve. After a specified skin-contact time, the sleeve were removed and the treated areas were thoroughly washed with flowing water. The animals were then observed for at least 7 days.

The products investigated were identified as follows:

(1) Hydrothol 191 N.B. 77-23-8 (23.4% Endothall)
(2) Sodium Endothall, N.B. 77-23-1 (15.8% Endothall)
(3) Potassium Endothall, N.B. 77-23-2 (28.3% Endothall)
(4) Herbicide 283, N.B. 77-23-4 (25.0% Endothall)

Results:

Product	Contact time	No. Rabbits Dead/Total	Time of Death
Hydrothol 191	3 hour	1/2	3 days
	2 hour	0/2	-
	1 hour	0/2	-
Sodium endothall	24 hour	0/2	-
Potassium endothall	1 hour	0/2	-
Herbicide 283	24 hour	2/2	<24 hour

Toxic Signs: All surviving animals refused food or water for three or four days after treatment which resulted in significant losses in body weight. These were restored within a week after food ingestion resumed.

Classification: Supplementary Data

(2.) Hydrothol 47 Granular. N.B. 72-23-7 (5.0% endothall)

Summary: Dermal Toxicity in Rabbits. Non-lethal at 200 mg/kg

Method: The fur was clipped from the trunks of three albino rabbits and the skin was moistened with a 1% solution of polysorbate 20. The sample was reduced to a fine powder and spread upon the trunk of each animal at the single dosage level of 200 mg/kg; this was covered with a wet 2-ply layer of gauze and overcovered with an impervious sleeve. After a skin contact period of 24 hours, the dressings were removed and the trunk of each animal was thoroughly washed with running water. The animals were then observed for 7 days.

Results: No deaths $LD_{50} > 200$ mg/kg

Toxic Signs: None produced

Body Weight: moderate loss in body weight but recovery within a week.

Classification: Supplementary Data

(1) LD_{50} was not determined and only 3 animals at one dose level were tested.

(3.) Hydout N.B. 77-23-6 (10.3% Endothall)

Summary: Dermal toxicity in Rabbits: Non-lethal at 200 mg/kg

Method: Fur clipped trunks of 3 albino rabbits and the skin was moistened with a 1% solution of polyporbate 20. The sample was reduced to a fine powder and spread upon the trunk of each animal at the single dosage level of 200 mg/kg; this was covered with a wet 2-ply layer of gauze and overcovered with an impervious sleeve. After a skin contact period of 24 hours, the dressings were removed and the trunk of each animal was thoroughly washed with running water. The animals were then observed for at least 7 days.

Results: No deaths $LD_{50} > 200$ mg/kg

Toxic Signs: Anorexia

Body Weight: loss for 3 or 4 days; recovery in 7 days.

Classification: Supplementary Data

(1) The LD_{50} was not determined and only 3 animals at one dose level were tested.

(4.) Sodium endothall N.B. 77-23-1 (15.8% Endothall) A clear, colorless liquid; ambient density = 1.133 g/ml.

Summary: Washing the eyes of rabbits 5 or 15 minutes following instillation did not alter the irritant reaction in any discernible manner.

Washed eye irritancy in rabbits:

Method: 0.1 ml of sample was placed in the conjunctival sacs of both eyes of each of 4 albino rabbits. One eye of two if these albino rabbits. One eye of two of these animals was washed 5 minutes later and one eye of the other two was washed 15 minute later; washing was accomplished with continuously flowing water directed under the eyelids for a period of one minute. The resulting reactions were scored periodically for 7 days.

Results: The reaction in all eyes included severe conjunctival inflammation and chemosis, iridal congestion, and delayed corneal clouding. In every animal the reaction in the washed eye was identical with that in the contralateral unwashed eye.

Classification: Core-Minimum Data

TOX Category I: DANGER

(5.) Accelerate N.B. 77-23-5 (5.5% Endothall) A clear, yellow liquid; ambient density = 1.147 gm/ml.

Summary: Washing the eyes of rabbits 5 or 15 minutes following instillation did not alter the irritant reaction in any discernible manner.

Method: 0.1 ml of sample was placed in the conjunctival sacs of both eyes of each of four albino rabbits. One eye of two of these animals was washed five minutes later and one eye of the other two animals was washed 15 minutes later; washing was accomplished with continuous flowing water directed under the eyelids for a period of one minute. The resulting reactions were scored periodically for seven days.

Results: The reaction in all eyes included severe conjunctival inflammation and chemosis, iridal congestion, and delayed corneal clouding. In every animal the reaction in the washed eye was identical with that in the contralateral unwashed eye.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 140. Letter and data J.C. Calandra to Obren Kackemet - June 3, 1976.

(✓) Hydrothol 191 (23.4% endothall - N.B. 77-28-2)

1. Acute Dermal Toxicity Study with Hydrothol 191 in Albino Rabbits (I.B.T. No. 8530-08497, 6/3/76)

Two groups of 4 rabbits (2M & 2F), one half abraded and one half unabraded, received 23.41 and 52.67 mg/kg for 24 hr. under an impervious cuff. Observations for 14 days. At 23.41 mg/kg, 2 out of 4 died; at 52.67 mg/kg, 4 out of 4 died.

Results: LD_{50} = 23.41 mg/kg (approximate)

Body Weight: loss after 14 days in survivors

Toxic Signs: muscular weakness, ataxia, prostation

Classification: Supplementary Data

(1) LD_{50} was not determined ~~accurated~~ accurately.

NOTE: This acute dermal dermal LD_{50} may exceed an RPAR criterion (less than 40 mg/kg as formulated). However the study is considerated as supplementary data.

Exhibit 141. Letter and data A.R. Latven to Obren Keckemet - August 12, 1975.

(Pharmacology Research, Inc.)

(6) Hydrothol 47 N.B. 58-194-8 (18.7%) An amber colored liquid; ambient density= .945 gm/ml.

Summary: (1) Acute Oral LD_{50} = 730 mg/kg (male rats) TOX CAT. III: CAUTION
(2) Acute Dermal LD_{50} = 160 mg/kg (rabbits) TOX CAT. I: DANGER
(3) Eye Irritation in Rabbits: corrosive, TOX CAT. I: DANGER
(4) Skin Irritancy in Rabbits: necrosis, TOX CAT. I: DANGER

(1) Acute Oral Toxicity in Rats.

Method: 5 groups of 5 male WBS/Wistar rats, 220 gm BW, were administered by stomach tube doses of 350, 500, 700, 1000 and 1400 mg/kg. Surviving animals were observed for 7 days.

Results: LD_{50} = 730 mg/kg (male rats)

Toxic Signs: General depression

Body Weight: Anorexia for one or two days, regained

Necropsy: not performed

Classification: Core-Minimum Data

TOX Category III: CAUTION

(2) Acute Dermal Toxicity in Rabbits.

Method: Three groups of 3 rabbits received aqueous dilutions of the sample at doses of 100, 140 and 200 mg/kg spread upon the skin of fur-clipped trunks and covered with impervious sleeves for 24 hr; all

(continue on next page)

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doses were contained in 2.0 ml/kg. Surviving animals were observed for seven days.

Results: LD_{50} = 160 mg/kg (Rabbits)

Toxic Signs: General depression; rabbits which succumbed were found in opisthotonic position. Survivors showed anorexia.

Necropsy: not performed

Classification: Core-Minimum Data

TOX Category I: DANGER

(3) Eye Irritancy in Rabbits.

Method: 0.1 ml of the undiluted sample was placed in the conjunctival sac of one eye of each of six albino rabbits. The resulting reactions were scored periodically for one week.

Results: corrosive; corneal opacity completely covered eye at 7 days. White discharge.

Classification: Core-Minimum Data

TOX Category I: DANGER

(4) Skin Irritancy in Rabbits.

Method: 0.5 ml of the undiluted sample was applied to one intact and one abraded skin site under standard gauze patches on opposite flanks on each of six albino rabbits. The entire fur-clipped trunk was then covered with an imprevious sleeve for an intended skin-contact period of 24 hours.

Results: All rabbits died overnight as a result of percutaneous toxicity. In all cases the treated sites were distinitly necrotic in appearance.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 142. Letter and data T.C. Calandra to Obren Keckemet - June 3, 1976 (Industrial Biotest; IBT#8530-08497) Acute Dermal Toxicity Studies with Herbicide 273 and Hydrothol 191 in Albino Rabbits.

(v) Test Material: Herbicide 273 (potassium endothall, 28.6% endothall - N.B. 77-28-1)

Method: Four groups of 4 rabbits (2M 7 2F) received 35.12, 52.67, 79.01 and 177.8 mg/kg of test material on fur clipped skin that was abraded in one half of the animals. Test material was covered with imprevious sleeves for 24 hr.

Results: LD_{50} = 35.12 mg/kg (approximate)

Toxic Signs: cyanosis, prostation, convulsions

Necropsy: not performed

Body Weight: Temporary loss in survivors

Classification: Supplementary Data

(1) LD_{50} was not accurately calculated. Both 35.12 & 79.01 mg/kg doses gave 50% mortality.

TOX Category I: DANGER

Exhibit 143. Letter and data A.R. Latven to Harold L. Lindabeny, September 9, 1971 (Pharmacology Research, Inc.)

(1.) Accelerate - a clear pale yellow liquid

Summary: TOX Category I: DANGER, corneal opacification, iridal congestion conjunctival inflammation and chemosis.

Eye Irritancy in Rabbits.

Method: 0.1 ml was placed in the conjunctival sac of one eye of each of 3 albino rabbits and the resulting reaction was scored up to 11 days thereafter.

Results: Instillation caused immediated blepharospasm and pain. Corneal opacity present at 11 days.

Classification: Core-Minimum Data

TOX Category I: DANGER

(✓) Exhibit 144. Report - The Acute Dermal LD_{50} of Hydrothol 191 liquid on New Zealand Albino Rabbits - Cannon Laboratories, Inc - May 4, 1977.

Method: Three groups of 4 albino (one-half abraded) rabbits (2M & 2F), 2.3-3.0 kg, received dermal applications of 50, 100 and 300 mg/kg of test material for 24 hours under an impervious cuff. The animals were observed daily for adverse reaction and survival for a period of 14 days.

Results: LD_{50} = 50 mg/kg (rabbits, both sexes)

Toxic Signs: Decreased activity, loss of righting reflex, edema, eschar, erythema and death.

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category I: DANGER

(1) Exhibit 145. Report - The effects of Hydrothol 191 Liquid on the eye mucosa of New Zealand Albino Rabbits - Cannon Laboratories - May 4, 1977.

Method: 0.1 ml of undiluted liquid was instilled into the left eye of 6 rabbits. The right eye served as a control. Treated eyes were observed and scored at 24, 48, 72 hours and 4 & 7 days after instillation.

Results: 3 animals dead by 72 hours. Corrosive and Complete corneal opacification at 7 days.

Classification: Core-Minimum Data

TOX Category I: DANGER

(✓) Exhibit 146: Report - A Primary Dermal Irritation Study of Hydrothol 191 Liquid on Abraded and Non-Abraded Skin of New Zealand Albino Rabbits - Cannon Labs., Inc., - April 12, 1977.

Method: 0.5 ml applied to abraded & non-abraded fur clipped skin sites on backs of 6 albino rabbits under an impervious cuff for 24 hour. Observations at 24 & 72 hours after exposure.

Results: All the test animals died before the 24 hour score. No scores were made.

Classification: Core-Minimum Data (a) Dermal LD_{50} results showed eschar at 24 hours.

TOX Category I: DANGER

(✓) Exhibit 147. Report - Oral LD_{50} in Rats - Cannon Laboratories Inc. - 5/11/77.

Test Material: Hydrothol 191 Liquid

Method: Six groups of 10 Sprague-Dawley rats (5M & 5F), 200-300 grams, received by intubation, doses of 50, 150, 250, 350, 450 and 500 mg/kg BW of test material. Observations for 14 days.

Results: LD_{50} = 221 mg/kg (both sexes)

Toxic Signs: decreased locomotor activity, piloerection, ptosis

Necropsy: greenish-white fluid in stomach

Body Weight: losses regained by survivors

Classification: Core-Minimum Data

TOX Category II: WARNING

(1) Exhibit 148. Report - Acute Inhalation Toxicity of Aquathol "K", Hydrothol 191 liquid, Hydrothol 47 liquid, Aquathol - Cannon Laboratories, Inc. - April 25, 1977.

Summary: Acute Inhalation Toxicity of

(a) Aquathol K; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION
(b) Hydrothol 191 Liquid; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION
(c) Hydrothol 47 Liquid; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION
(d) Aquathol; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION
(e) Des-i-CATE Accelerate; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION
(f) Knox-out 2 FM; $LC_{50} > 20$ mg/L TOX Category IV: CAUTION

Method: Ten rats (5M & 5F) were exposed for 1 hr. to a nominal concentration of 20 mg/L of test material in a 40 L glass exposure chamber. Observation for 14 days.

Results: 1 hr. concentration

(a) Aquathol K; 4/10 died at 20.78 mg/L
(b) Hydrothol 191 Liquid; 4/10 died at 22.12 mg/L
(c) Hydrothol 47 Liquid; 5/10 died at 20.47 mg/L
(d) Aquathol; 2/10 died at 20.97 mg/L
(e) Des-i-cate Accelerate; 2/10 died at 21.87 mg/L
(f) Knox-OUT 2 FM; 0/10 at 22.42 mg/L

Toxic Signs: All groups - grooming, eye membrane irritation, lacrimation labored respiration, salivation, blood around eyes and nose.

Necropsy: All groups - slight to moderate lung congestion & hemorrhage, mucousin trachea.

Body Weight: Losses regained by survivors.

Classification: Core-Minimum Data

(a) LD_{50} was not accurately determined.

TOX Category IV: CAUTION

Exhibit 149. Report - The Acute Dermal LD_{50} of Hydrothol 47 liquid on New Zealand Albino Rabbits - Cannon Laboratories, Inc. - April 12, 1977.

(✓) Test Material: Hydrothol 47 liquid

Method: 4 groups of 4 New Zealand albino rabbits (2 males & 2 females), 2.3-3.0 kg BW, received dermal applications of 50, 100, 300 and 500 mg/kg of test material (one-half of animals were abraded) under an imprevious cuff for 24 hours. Observations were for 14 days.

Results: LD_{50} = 300 mg/kg (both sexes)

Toxic Signs: eschar at skin sites.

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 150 - Report - The effects of Hydrothol 47 liquid on the eye mucosa of New Zealand Albino Rabbits - Cannon Laboratories, Inc - April 12, 1977.

Test Material: Hydrothol 47 liquid

Method: 0.1 ml of test material was instilled in the left eye of 6 New Zealand Albino rabbits 2.0-2.5 kg BW, with the right eye serving as a control. The treated eyes were observed and scored at 24, 48 & 72 hours as well as 4 & 7 days.

Results: Mortality in 2 rabbits at 72 hours maximum score - corrosive, corneal opacity in all rabbits at 7 days.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 151 Report - A primary Dermal Irritation Study of Hydrothol 47 liquid on Abraded and Non-Abraded Skin of New Zealand Albino Rabbits - Cannon Laboratories - April 12, 1977.

Test Material: Hydrothol 47 liquid

Method: 0.5 ml of test material was applied to abraded and non-abraded test sites on fur clipped trunk of six albino rabbits for 24 hours under an impervious cuff. Observation at 24 & 72 hours after exposure for evaluation.

Results: All the test animals died before the 24 hour score.

Classification: Core-Minimum Data

(a) Survivors of Dermal LD_{50} with Hydrothol 47 showed necrotic eschar lesions at 24 hours.

TOX Category I: DANGER

Exhibit 152 Report of Oral LD_{50} in Rats - Cannon Laboratories, Inc - May 11, 1977.

Test Material: Hydrothol 47 liquid (10% aqueous solution)

Method: Five groups of 10 Sprague-Dawley rats (5M & 5F), 200-300 gm BW, were administered by oral intubation a 10% aqueous solution of 200, 350, 500, 1000 and 5000 mg/kg body weight of test material. Observation for 14 days.

Results: LD_{50} = 381 mg/kg (both sexes)

Toxic Signs: All deaths in 1st day, ptosis, piloerection, decreased activity, death.

Necropsy: Hemorrhage of stomach

Body Weight: Losses regained after one week.

Classification: Core-Minimum Data

(a) Test material was a 10% solution of Hydrothol 47 liquid, not undiluted formulation.

TOX Category II: WARNING

Exhibit 153 - The effects of Aquathol K on the eye mucosa of New Zealand Albino Rabbits - Cannon Laboratories, Inc - April 12, 1977.

Test Material: Aquathol K liquid

Method: 0.1 ml of test material was instilled into the left eye of six albino rabbits, 2.0-2.5 kg BW, with the untreated right eye serving as a control. The treated eyes were observed periodically for 7 days.

Results: Corneal opacity irreversible in all rabbits at 7 days conjunctivitis.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 154 - Report - A Primary Dermal Irritation Study of Aquathol K on abraded and non-abraded skin of New Zealand Albino Rabbits, Cannon Laboratories, Inc. - May 4, 1977.

Test Material: Aquathol K Liquid

Method: 0.5 ml of test material was applied dermally to abraded and non-abraded test sites on backs of six albino rabbits under an impervious cuff for 24 hours. Observation at 24 & 72 hours after exposure.

Results: Slight erythema and edema were exhibited on one skin site at 24 hours. No irritation was exhibited at 72 hours.

Classification: Core-Minimum Data

TOX Category IV: CAUTION

Exhibit 155 - Report - The Acute Dermal LD_{50} of Aquathol K on New Zealand Albino Rabbits - Cannon Laboratories, Inc - May 4, 1977.

Test Material: Aquathol K liquid

Method: Three groups of 4 New Zealand Albino rabbits (2M & 2F), 2.3-3.0 kg BW, received dermal application of 2, 5 and 10 gm/kg test material on fur clipped trunk (one-half of animals were abraded) for 24 hours under an impervious cuff. Observation for 14 days.

Results: one death at 10 gm/kg
$LD_{50} > 10$ gm/kg (both sexes)

Toxic Signs: erythema and edema of skin

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 156 - Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc. - May 10, 1977.

Test Material: Aquathol K liquid

Method: Five groups of 10 Sprague-Dawley rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 60, 70, 100, 250 and 5000 mg/kg BW of test material. Observation for 14 days.

Results: LD_{50} = 280 mg/kg (both sexes)

Toxic Signs: decreased activity, ptosis, piloerection

Necropsy: no abnormal gross changes

Body Weight: Survivors regained BW in 2 days.

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 157 - Report - The effects of Aquathol on the Eye Mucosa of New Zealand Albino Rabbits - Cannon Laboratories, Inc - April 12, 1977.

Test Material: Aquathol liquid

Method: 0.1 ml of test material was instilled into the conjunctival sac of the left eye of six New Zealand albino rabbits, 2.0-2.5 kg, with the untreated right eye serving as a control. The treated eyes were scored periodically up to 7 days.

Results: At 4 days, 6/6 rabbits showed corneal opacity. At 7 days, 1/6 rabbits showed corneal opacity and conjunctivitis. The remaining five rabbits showed no irritation in cornea, iris or conjunctival. The score of 1 was given to the corneal opacity present in the rabbit at day 7.

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 158 - Report - A Primary Dermal Irritation Study of Aquathol on Abraded and Non-Abraded Skin of New Zealand Albino Rabbits - Cannon Laboratories, INc - April 12, 1977.

Test Material: Aquathol liquid

Method: 0.5 ml of test material was applied dermally to the abraded and non-abraded skin of fur clipped trunks of six albino rabbits under an imprevious cuff for 24 hours. Observation was at 24 & 72 hours after exposure.

Results: No irritation at 24 or 72 hours.

Classification: Core-Minimum Data

TOX Category IV: CAUTION

Exhibit 159 - Report - The Acute Dermal LD_{50} of Aquathol on New Zealand Albino Rabbits - Cannon Laboratories, Inc - May 4, 1977.

Test Material: Aquathol liquid

Method : Three groups of 4 New Zealand albino rabbits (2M & 2F), 2.3-3.0 kg BW, received 2, 5 and 10 gm/kg BW doses of Aquathol on fur clipped backs(one half of the animals were abraded) under an imprevious cuff for 24 hours. Observation for 14 days.

Results: LD_{50} = 5.0 gm/kg (both sexes)

Toxic Signs: edema, erythema

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 160 - Report on Oral LD_{50} in Rats - Cannon Laboratories Inc - May 4, 1977.

(v) Test Material: Aquathol

Method: Five groups of 10 Sprague-Dawley rats (5M & 5F) received by oral intubation 150, 250, 350, 450 and 5000 mg/kg BW doses of test material. Observation was for 14 days.

Results: LD_{50} = 329 mg/kg (both sexes)

Toxic Signs: decreased activity, ptosis, piloerection

Body Weight: Losses regained within 5 days

Necropsy: No outstanding gross pathology

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 161 - Report - A Primary Dermal Irritation Study of Aquatol Granular on Abraded and Non-Abraded Skin of New Zealand Albino Rabbits - Cannon Laboratories, Inc - April 12, 1977.

(v) Test Material: Aquathol Granular

Method: 0.5 gm of test material was applied dermally to abraded & non-abraded fur clipped skin of backs of six male albino rabbits under an imprevious cuff for 24 hours. Observations were made at 24 & 72 hours after exposure.

Results: No irritation at 24 or 72 hours

Classification: Core-Minimum Data

TOX Category IV: CAUTION

Exhibit 162 - Report - The effects of Aquathol Granular on eye muscosa of New Zealand Albino Rabbits - Cannon Laboratories, Inc - May 2, 1977.

Test Material: Aquathol Granular

Method: 0.1 gm of test material was instilled (ground up in a motar by pestle for about 3 hours before administrations) into the conjunctival sac of the left eye, with the untreated right eye serving a control, of six New Zealand albino rabbits, 2.0-2.5 kg BW. Observation was made periodically for 7 days.

Results: Corneal opacity present in all treated eyes (6/6) at 7 days; conjunctivitis & iritis present at 7 days. Corrosive.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 163 Report - The Acute Dermal LD_{50} of Aquathol Granular on New Zealand Albino Rabbits.

Test Material: Aquathol Granular

Method: Three groups of 4 rabbits (2M & 2F) received 2, 5 and 10 gm/kg of test material on fur clipped trunks (one-half of animals were abraded) under an imprevious cuff for 24 hours. Observation was for 14 days.

Results: $LD_{50} > 10$ gm/kg (both sexes) no deaths

Body Weight: not reported

Necropsy: not reported

Toxic Signs: No toxic signs occurred

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 164 Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc - May 11, 1977.

Test Material: Aquathol Granular

Method: Five groups of 10 Sprague-Dawley Rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 100, 500, 1000, 2500, and 5000 gm/kg of test material. Observation was for 14 days.

Results: LD_{50} = 1340 mg/kg (both sexes)

Toxic Signs: loss of righting reflex, ptosis, death

Body Weight: Regain in body weight within 7 days.

Necropsy: No outstanding gross pathological changes.

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 165-Report A Primary Dermal Irritation Study of Hydrothol 191 Granular on Abraded and Non-Abraded Skin of New Zealand Albino Rabbits. Cannon Laboratories, Inc. April 12, 1977.

(1) Test Material: Hydrothol 191 Granular

Method: 0.5 gm of test material was applied dermally to abraded and non-abraded surfaces on fur clipped backs of six male Albino rabbits, 2.0-2.5 kg BW, under an impervious cuff for 24 hours. Observation at 24 and 72 hours after exposure.

Results: No irritation was exhibited at 24 or 72 hours.
Classification: core-minimum data, TOX CATEGORY IV: CAUTION

Exhibit 166 - Report The Effects of Hydrothol 191 Granular on the eye mocosa of New Zealand Albino Rabbits. Cannon Laboratories, Inc. - May 2, 1977.

Test Material: Hydrothol 191 Granular

Method: 0.1 gm of test material (ground up in a motar by pestle for 3 hrs.) was instilled in the conjunctival sac of the left eye with the right eye serving as an untreated control in Six New Zealand Albino Rabbits, 2.0-2.5 kg BW. Observations were made periodically for 7 days.

Results: Corrosive; severe corneal opacity in all rabbits (6/6) at 7 days iritis, conjunctivitis also present.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 167 Report - The Acute Dermal LD_{50} of Hydrothol 191 Granular on New Zealand Albino Rabbits. Cannon Laboratories, Inc. May 4, 1977.

Test Material: Hydrothol 191 Granular

Method: Three groups of 4 New Zealand albino rabbits (2M & 2F), 2.3-3.0 kg BW, received dermally doses of 2, 5 and 10 gm/kg BW of test material on fur clipped trunks (one half of the animals were abraded) for 24 hours under an impervious cuff. Observation was for 14 days.

Results: No deaths $LD_{50} > 10$ gm/kg

Toxic Signs: edema, erythema

Body Weight: not reported

Necropsy: no t reported

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 168 - Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc. - May 11, 1977.

Test Material: Hydrothol 191 Granular (10% Suspension)

Method: Five groups of 10 Sprague-Dawley rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 1000, 2000, 3000, 4000 and 5000 mg/kg BW as a 10% suspension in distilled water. Observation was for 14 days.

Results: LD_{50} = 1540 mg/kg (both sexes)

Toxic Signs: decreased motor activity, ptosis, piloerection

Body Weight: Body weight lossess regained after 7 days.

Necropsy: No outstanding gross pathological changes.

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 169 Report - A Primary Dermal Irritation Study of Hydrothol 47 Granular on Abranded and Non-Abraded skin of New Zealand Albino Rabbits - Cannon Laboratories, INc. - April 12, 1977.

(J.) Test Material: Hydrothol 47 Granular

Method: 0.5 gm of test material was applied dermally tp abraded and non-abraded skin sites on fur clipped back of six New Zealand Albino rabbits, 2.0-2.5 kg under an impervious cuff for 24 hrs. Observations at 24 and 72 hour after exposure.

Results: mild edema on abraded skin at 24 hours; no irritation at 72 hours.

Classification: Core-Minimum Data

TOX Category IV: CAUTION

Exhibit 170 Report - The effects of Hydrothol 47 Granular on the eye mucosa of New Zealand Albino Rabbits - Cannon Laboratories, Inc., May 2, 1977.

Test Material: Hydrothol 47 Granular

Method: 0.1 gm of test material (ground up in a mortar by pestle for 3 hours) was instilled in the conjunctival sac of the left eye of six New Zealand albino rabbits, 2.0-2.5 kg BW, with the untreated right eye serving as a control. The treated eyes were scored periodically for 7 days.

Results: Complete corneal opacity iritis and conjunctivitis at 7 days.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 171 Report - The Acute Dermal LD_{50} of Hydrothol 47 Granular on New Zealand Albino Rabbits - Cannon Laboratories, Inc. - May 4, 1977.

Test Material: Hydrothol 47 Granular - ground-up with mortar and pestle before used.

Method: Three groups of 4 New Zealand albino rabbits (2M & 2F) per group, 2.3-3.0 kg BW, received dermally doses of 2, 5 and 10 gm/kg BW on the fur clipped trunks (one half of the animals were abraded) for 24 hours under an impervious cuff. Observation was for 14 days.

Results: No deaths, $LD_{50} > 10$ gm/kg (both sexes)

Toxic Signs: erythema

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 172-Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc., May 11, 1977.

Test Material: Hydrothol 47 Granular - a 10% suspension in distilled water.

Method: Five groups of 10 Sprague-Dawley rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 250, 500, 1000, 2000 and 5000 mg/kg BW of test material. Observation was 14 days.

Results: LD_{50} = 1860 mg/kg (both sexes)

Toxic Signs: decreased locomotor activity, piloerection ptosis, death.

Body Weight: Body weight lossess regained in 5 days.

Necropsy: No outstanding gross pathological organ changes.

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 173. Report - The effects of Hydrothol on the eye mucosa of New Zealand Albino rabbits - Cannon Laboratories, INc., April 12, 1977.

Test Material: Hydout TM (N.B. 77-99-5)

Method: 0.1 gm of test material was instilled intc tne conjunctival sac of the left eye of six New Zealand albino rabbits, 2.0-2.5 kg BW, with the untreated right eye serving as a control. Observations were made periodically for 7 days.

Results: Complete corneal opacity iritis, conjunctivitis in all rabbits (6/6) at 7 days. Corrosive.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 174. Report - A Primary Dermal Irritation Study of Hydout on Abraded and Non-Abraded skin of New Zealand Albino Rabbits - Cannon Laboratories, Inc., April 12, 1977.

Test Material: Hydout (TM)

Method: 0.5 gm of test material was applied dermally to abraded and non-abraded skin sited on fur clipped trunks of six New Zealand albino rabbits under an impervious cuff for 24 hours. Observations were at 24 and 72 hours after exposure.

Results: erythema and edema in abraded skin at 24 hours in 3/6 rabbits. No irritation at 72 hours.

Classification: Core-Minimum Data

TOX Category IV: CAUTION

Exhibit 175. Report - The Acute Dermal LD_{50} of Hydout on New Zealand Albino Rabbits - Cannon Laboratories, Inc., May 4, 1977.

Test Material: Hydout (TM)

Method: Three groups of 4 albino New Zealand rabbits (2M & 2F), 2.3-3.0 kg BW, received dermally doses of 2, 5 and 10 gm/kg BW of test material (one-half of animals were abraded) under an impervious cuff for 24 hours. Observation was for 14 days.

Results: No deaths, $LD_{50} > 10$ gm/kg

Toxic Signs: normal

Body Weight: not reported

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 176. Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc., May 11, 1976.

Test Material: Hydout (TM) 10% solution in distilled water.

Method: Five groups of 10 Sprague-Dawley Rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 100, 500, 1000, 2000 and 5000 mg/kg BW of 10% aqueous solution of test material. Observation for 14 days.

Results: LD_{50} = 600 mg/kg (both sexes)

Toxic Signs: decreased locomotor activity, ptosis

Body Weights: Losses regained within 3 days.

Necropsy: pale kidney in 5000 mg/kg group

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 177 Report - The effects of Des-i-cate/Accelerate on the eye mucosa of New Zealand albino rabbits - Cannon Laboratories Inc., April 12, 1977.

(v) Test Material: Des-I-cate/Accelerate

Method: 0.1 ml of test material was instilled into the conjunctival sac of the left eye of Six New Zealand albino rabbits, 2.0-2.5 kg BW, with the untreated right eye serving as a control. Observations were made periodically for 7 days.

Results: Corrosive (2/6) rabbits died at 72 hours. Complete 6 corneal opacity, iritis, conjunctivitis in survivors at 7 days.

Classification: Core-Minimum Data

TOX Category I: DANGER

Exhibit 178 Report - The Acute Dermal LD_{50} of Des-I-cate/Accelerate on New Zealand Albino Rabbits - Cannon Laboratories, Inc., May 4, 1977.

Test Material: Des-I-Cate/Accelerate

Method: Three groups of 4 rabbits (2M & 2F) received cermally on fur clipped trunks (one half of animals abraded ccses of 100, 300 and 500 mg/kg BW under an impervious cuff for 24 hours. Observations were for 14 days.

Results: LD_{50} = 300 mg/kg (both sexes)

Body Weight: not reported

Toxic Signs: decreased locomotor activity, edema, eschar

Necropsy: not reported

Classification: Core-Minimum Data

TOX Category II: WARNING

Exhibit 179. Report on Oral LD_{50} in Rats - Cannon Laboratories, Inc., May 4, 1977.

Test Material: Des-I-Cate/Accelerate

Method: Five groups of 10 Sprague Dawley rats (5M & 5F), 200-300 gm BW, received by oral intubation doses of 250, 500, 750, 1000, and 5000 mg/kg BW of test material. Observation was for 14 days.

Result: LD_{50} = 800 mg/kg (both sexes)

Body Weight: Losses regained in 6 days

Toxic Signs: decreased locomotor activity, ptosis, death

Necropsy: Thickening of pyloric stomach, hemorrahaging lungs .

Classification: Core-Minimum Data

TOX Category III: CAUTION

Exhibit 180. Report - Acute Inhalation Toxicity of Aqualthol Granular, Hydrothol 191 Granular, Hydrothol 47 Granular, Hydout - Cannon Laboratories, Inc., May 23, 1977.

1. LC_{50} of Aquathol Granular

Test Material: Aquathol Granular

Method: Three groups of 10 rats (5M & 5F), 200-300 gms, were exposed to test material in a 40-L chamber at doses of 1.5, 2.5 and 16.66 mg/L for one hour. Observations were for 14 days.

Results: LC_{50} = 2.26 mg/L (both sexes)

Toxic Signs: Grooming, labored respiration, eye membrane irritation, inactivity, corneal opacity.

Body Weight: Weight losses regained after 7 days.

Necropsy: hemorrhage on lungs, mucous in lungs.

Classification: Core-Minimum Data

TOX Category III: CAUTION

2. Test Material: Hydrothol 191 Granular

Method: Three groups of 10 rats (5M & 5F), 200-300 gmd, were exposed to test material in a 40-L chamber at doses of 1.9, 6.1 and 9.5 mg/L for one hour. Observations were for 14 days.

Results: LC_{50} = 5.32 mg/L (both sexes)

Toxic Signs: Grooming, eye membrane irritation, inactivity, corneal opacity, laboraed respiration.

Body Weight: Weight losses regained after 7 days.

Necropsy: hemorrahage on lungs, mucous in lungs and trachea.

Classification: Core-Minimum Da[illegible].

TOX Category II: CAUTION

3. Test Material: Hydrothol 47 Granular

Method: Three groups of 10 rats (5M & 5F), 200 to 300 gm BW, were exposed to test material in a 40-L chamber at doses of 1.2, 2.3 and 4.1 mg/L for one hour. Observations were for 14 days.

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Results: LC_{50} = 2.30 mg/L (both sexes)

Toxic Signs: Grooming, eye membrane irritation, inactivity, labored respiration.

Body Weight: Losses regained slowly.

Necropsy: hemorrahage on lungs, mucous in lungs and trachea.

Classification: Core-Minimum Data

TOX Category III: CAUTION

(1) 4. Test Material: Hydout

Method: Three groups of 10 rats (5M & 5F), 200-300 gm BW, were exposed to test material in a 40-L chamber at doses of 2.2, 3.7, 5.4 mg/L for one hour. Observations were for 14 days.

Results: LC_{50} = 3.70 mg/L (both sexes)

Toxic Signs: Grooming, eye membrane irritation, inactivity, labored respiration.

Body Weight: Recovered slowly

Necropsy: hemorrahage on lungs, mucous in lungs and trachea.

Classification: Core-Minimum Data

TOX Category III: CAUTION

TOX/HED:th:R.Engler:10-20-78

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