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

MEMORANDUM:

005619

SUBJECT: Evaluation of five acute toxicity studies with formulations, Diquat Water Weed Killer or Diquat 2 Spray

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

FROM: Krystyna K. Locke, Toxicologist
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

Krystyna K. Locke 12/10/86

TO: Richard F. Mountfort
Product Manager (23)
Registration Division (TS-767)

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

Budd 12/10/86

EPA ID Number: 239-1663
Record Number: 184987

Tox. Chem Number: 402
Project Number: 7-0179

Toxicology Branch/HED has completed an evaluation of the following studies:

Study type, number, and MRID	Accession No.	LD_{50}, LC_{50} or PIS	Toxicity Category	Core Grade
1. Acute oral LD_{50}- rat; SOCAL 1396; 5/10/79; 00081-506	098973	810 mg/kg (M) 600 mg/kg (F)	III	Minimum
2. Acute dermal LD_{50} - rabbit; SOCAL 1478; 7/7/80; 00100614	247358	288.5 mg/kg (M&F)	II	Guideline
3. Acute inhalation LC_{50}- rat; SOCAL 2353; 10/20/85; No MRID	263853	0.97 mg/L (M&F)	III	Guideline
4. Primary eye irritation - rabbit; SOCAL 901A; 7/13/76; 00081507	098973	No corneal opacity or iritis. Slight discharge present in 3/6 rabbits on day 14.	II	Minimum
5. Primary dermal irritation - rabbit; SOCAL 1479; 8/29/79; 0010793	247358	PIS = 0.9	IV	Guideline

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Studies #1 and 4 were first evaluated in 1981 (See T.B. memorandum dated 3/23/81; attached) and these reviews are still valid. Diquat 2 Spray was tested in study #4 and Diquat Water Weed Killer in the remaining studies. All of the studies were conducted by Chevron Environmental Health Center, Richmond, CA.

Because both formulations (end-use products) are very similar in composition to diquat technical (TGAI; see Chevron's memorandum dated 10/30/86; attached) the above studies were evaluated - at Chevron's request-to determine if they could fill data gaps for the acute studies listed in the Diquat Registration Standard. Based on the above reviews, acute studies with diquat technical are not required.

Attachments

Reviewed by: Krystyna K. Locke
Section II, Tox. Branch (TS-769C)
Secondary reviewer:
Section , Tox. Branch (TS-769C)

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DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation LC_{50} TOX. CHEM. NO.: 402

ACCESSION NUMBER: 263853 MRID NO.: None

EPA REGISTRATION NO.: 239-1663

TEST MATERIAL: Diquat Water Weed Killer (SX-1574); 19.5% diquat cation; 35.30% dibromide salt. PROJECT NO. 7-0179

SYNONYMS: None

STUDY NUMBER(S): SOCAL 2353

SPONSOR: Chevron Chemical Company, Agricultural Chemicals Division, Richmond, CA

TESTING FACILITY: Chevron Environmental Health Center, Inc., Richmond, CA

TITLE OF REPORT: The acute inhalation Toxicity of Diquat Water Killer (SX-1574) in rats.

AUTHOR(S): E.D. Bruce, L.C. Griffis and Z.A. Wong.

REPORT ISSUED: October 20, 1985.

CONCLUSIONS: LC_{50} = 0.97 mg/L (males and females), expressed as test material. Dose-related lesions were observed grossly and histologically in the lungs of both sexes.

Classification: Core-Guideline.

EXPERIMENTAL PROCEDURES

Sprague-Dawley rats (age: 65-91 days; weight: males, 313-493g and females, 197-314g), 5 males and 5 females per dose levels, were exposed (whole body) to aerosolized test material for 4 hours and then were sacrificed 14 days later. The dose levels used (target concentrations of the test material) were 0.0, 0.15, 1.0 and 4.0 mg/L. The volume of the inhalation chamber was 120 L and the average air-flow 4.6-11.0 L/min. The mean chamber temperature and relative humidity were 20.6-22.6°C and 63-73%, respectively. The mass mediam aerodynamic diameter of the aerosolized paticles ranged from 2.0 to 2.8 um and about 97-99% of the particles were smaller than 10 um. The rats were obtained from Bantin and Kingman, Inc., and were acclimated for 21-46 days before assignment to test group by a computer (Taussky-Tood overflow procedure). The rats received unrestricted amounts of food (Purina Laboratory Rodent Chow # 5001) and water, and were housed individually before, during and after exposure. The following parameters were examined: mortality, toxic signs, body weight gains, necropsy and histopathology (lungs and tracheas only).

RESULTS

The target or theoretical concentrations of Diquat Water Weed Killer in the inhalation chamber (0.15, 1.0 and 4.0 mg/L) were very similar to the analytical concentrations (0.16, 1.1 and 3.9 mg/L, respectively). Based on chemical analysis these dosage levels correspond to 0.86, 118 and 211 ug of diquat cation /L, respectively.

Mortality:

There were no deaths in the control and the low-dose groups, whereas all rats died in the high-dose group. In the mid-dose group, 3 males and 2 females died. Deaths occurred within the following days after the termination of the exposure: mid-dose males and females, 3-5; high-dose males, 2-10; and high-dose females, 7-9.

Toxic signs:

Signs of toxicity observed included: Weakness; squinted eyes; salivation; red nasal, oral, and ocular discharge; labored breathing; increased respiration rate; abnormal respiratory sounds; reduced food intake; reduced feces; soft stools or diarrhea; slight hindquarter ataxia; sores or alopecia on the throat; yellow or brown anogenital discharge; and an unkempt appearance. Squinted eyes were observed during exposure whereas the remaining signs were observed after exposure.

Body weights:

On day 14, both the control and the low-dose groups gained weight (males 63-71g and females, 26-32g), whereas the mid-dose group lost weight (males, 70g and females, 27g). The high-dose males and females lost 70 g and 50 g, respectively, on day 2 after exposure. These data indicate that weight gains were dose-related.

Necropsy:

With the exception of lungs and trachea, nothing remarkable was observed in all test groups. Regarding the lungs, reddening, darkening, edema, mottling, and consolidations were observed in the 1.1 mg/L and 3.9 mg/L dose groups. Two males in the 3.9 mg/L group had yellow fluid in the trachea.

Histopathology:

No abnormalities were observed in the control group. Three male and two female rats in the 0.16 mg/L group had slight inflammation and alveolar/septal thickening of the lungs. Dose-related inflammation, congestion, edema, and alveolar/septal thickening were observed in all animals from the 1.1 mg/L and 3.9 mg/L groups. The severity of the histologic lesions seen in the lungs was dose-related.

Quality assurance statement and analytical methology have been included in the submission.

The LC_{50} values and slopes, and their 95% confidence limits, determined by the method of Berkson*, were as follows:

	LC_{50} (95% Confidence Limits)	Slope (95% Confidence Limits)
Based on Total Aerosol Concentrations of Diquat Water Weed Killer (SX-1574):		
Males:	0.80 (0.002-419.44) mg/L	3.49 (0.005-2646.59)
Females:	1.09 (0.002-756.12) mg/L	3.68 (0.003-5091.58)
Combined:	0.97 (0.02-45.96) mg/L	2.72 (0.07-110.42)

*Berkson, J. Tables for use in estimating the normal distribution function by normit analysis. Biometrika, 44: 411-435, 1957.

Based on Diquat cation concentrations:

Males:	121 (18-793) ug/L	1.45 (0.18-11.99)
Females:	132 (22-781) ug/L	1.43 (0.22-9.40)
Combined:	125 (41-377) ug/L	1.33 (0.46-3.89)

Classification: Core-Guideline.

Reviewed by: Krystyna K. Locke
Section II, Toxicology Branch (TS-769C)
Secondary reviewer:
Section , Toxicology Branch (TS-769C)

005619

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal LD_{50} TOX. CHEM. NO.: 402

ACCESSION NUMBER: 247358 MRID NO.: 00100614

EPA REGISTRATION NO.: 239-1663 PROJECT NO.: 7-0179

TEST MATERIAL: Diquat Water Weed Killer (SX-1165)

SYNONYMS: None

STUDY NUMBERS: SOCAL 1478/S-1623

SPONSOR: Chevron Chemical Company, Agricultural Chemicals Division, Richmond, CA

TESTING FACILITY: Chevron Environmental Health Center, Richmond, CA

TITLE OF REPORT: The Acute Dermal Toxicity of Diquat Water Weed Killer in Adult Male and Female Rabbits

AUTHORS: C.H. Bullock and Z.A. Wong

REPORT ISSUED: July 7, 1980

CONCLUSIONS:

LD_{50} = 288.5 mg/kg, expressed as test material (males and females). The test material caused various gross and histopathologic changes in the skin, lungs, liver, and kidneys.

Classification: Core-Guideline.

EXPERIMENTAL PROCEDURES

Single doses of the test material--0, 50 (males only), 500, 1000, 2000, or 5000 mg/kg--were applied on the trunks of New Zealand rabbits (age: 10 to 14 weeks; weight: 2.0 to 3.2 kg) and the application sites were occluded. There were five males and five females, all with abraded skin, in the 5000 mg/kg group, whereas there were six males and six females (three with abraded and three with unabraded skin) in the remaining groups. The exposure time was 24 hours and the test material was wiped off at the end of the exposure. The observation time was 14 days; collars were placed on the animals for 7 days to prevent ingestion of the test material. The animals were housed singly at 21 °C (relative humidity, 41 to 77 percent); were fed restricted amounts of food (about

115 g/day of Purina Laboratory Rabbit Chow) and unrestricted water; were weighed weekly; and all were necropsied.

RESULTS

Mortality - All males and most females died in the 500 to 5000 mg/kg groups. Most females died within 17 to 70 minutes and most males died within 2 to 8 days after exposure.

Toxic signs - At the lowest levels tested, the only toxic sign in males and females was a decreased food consumption. The following toxic signs were observed in the remaining groups: ataxia, weakness, collapse, labored respiration, depression, decreased food consumption, hematuria, and diarrhea.

Body weight gains - All animals were weighed weekly, but body weights were reported only for the surviving males. On observation day 14, the average weight gains of the rabbits in the control and the 50 mg/kg diquat-treated groups were 280 g and 400 g, respectively. However, the control and the 100 mg/kg diquat-treated groups gained 200 g and 10 g, respectively. (The 50 mg/kg group had a separate control group.)

Necropsy - Most of the treated rabbits had (1) thick and necrotic (escharotic) skin (not stated whether at the site of application); (2) discolored (red or pale), enlarged, and mottled kidneys; (3) congested, mottled, or necrotic livers with pale areas; and (4) congested, edematous and red lungs with raised foci, white masses, or gray areas. (Individual data were reported.)

Histopathology - The following findings were observed in most of the treated rabbits.

1. Skin - Epidermal necrosis, diffuse acanthosis, diffuse hyperkeratosis, and scab formation.

2. Lungs - Collapse of alveoli, diffuse acute pulmonary edema, and diffuse acute interstitial pneumonia.

3. Liver - Centrolobular vacuolar degeneration and multifocal acute necrotizing hepatitis.

4. Kidneys - Diffuse acute tubular necrosis.

A quality assurance statement has been included in the submission.

The LD_{50} values and slopes and their 95 percent confidence limits determined by the method of Berkson* were as follows:

	LD_{50} (95% Confidence Limits)**	Slope (95% Confidence Limits)
Males:	262 (75 to 915) mg/kg	4.3 (1.5 to 12.5)
Females:	315 (44 to 2260) mg/kg	5.0 (0.67 to 36.9)
Combined:	288.5 mg/kg	

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* Berkson, J. Tables for use in estimating the normal distribution function by normit analysis. Biometrika 44: 411-435, 1957.

** Expressed as Diquat Water Weed Killer (SX-1165).

Classification: Core-Guideline.

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Reviewed by: Krystyna K. Locke
Section II, Tox. Branch (TS-769C)
Secondary reviewer:
Section , Tox. Branch (TS-769C)

DATA EVALUATION REPORT

STUDY TYPE: Primary dermal irritation TOX. CHEM. NO.: 402

ACCESSION NUMBER: 247358 MRID NO.: 00107903

EPA REGISTRATION NO.: 239-1663

TEST MATERIAL: Ortho Diquat Water Weed Killer (S-1624) PROJECT NO.: 7-0179

SYNONYMS: None

STUDY NUMBER(S): SOCAL 1479

SPONSOR: Chevron Chemical Company, Agricultural Chemicals Division, Richmond, CA

TESTING FACILITY: Chevron Environmental Health Center, Inc., Richmond, CA

TITLE OF REPORT: The skin irritation potential of Diquat Water Weed Killer

AUTHOR(S): J.E. Levy, Z.A. Wong and J.A. MacGregor

REPORT ISSUED: August 29, 1979.

CONCLUSIONS: The test material was a slight skin irritant to rabbits. PIS = 0.9.

Classification: Core-Guideline.

EXPERIMENTAL PROCEDURES

The test material (a dark amber liquid, coded SX-1165), 0.5 ml, was applied on both the intact and abraded backs of 6 adult, male New Zealand rabbits and the application sites were occluded. The animals were acclimated for 2 weeks and were 12-22 weeks old at the start of the test. The exposure time was 24 hours after which the application sites were wiped. The rabbits were housed singly at 21°C and relative humidity of 44 to 77%, and received restricted amounts of food (Purina Laboratory Chow, about 115g/day) and unrestricted water. Scoring was performed by the procedure of Draize* at 1,2,3,4 and 7 days following application of the test material.

RESULTS

According to the authors, the test material caused very slight to well-defined erythema through 48 hours in most rabbits. One rabbit displayed very slight edema in the abraded test site area at 24 hours. Irritation was reduced in most rabbits at 72 hours and no irritation was observed by the 96-hours reading. Individual data were submitted in support of these statements. There was no difference in toxic response between intact and abraded skin.

The primary irritation score was 0.9.

*Draize, J.H., G. Woodward and H. O. Calvery. Methods for the study of irritation and toxicity of substances applied topically to skin and mucous membranes. J. Pharmacol. Exptl. Therap., 82:377-390, 1944.