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

003735

4-4-84

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Tox. Chem. No. 96

DATE:

SUBJECT: Review of the Toxicity Data on Triox Vegetation Killer and
Its Signal Word Change. EPA I.D. #239-2381

TO: Robert Taylor, Jr. (PM #25)
Registration Division (TS-767C)

THRU: William M. Butler, Jr., Head
Review Section III
Toxicology Branch (TS-769C)
and

*William M. Butler Jr. 3-26-84
11 p.m. 4/1/84*

William Burnam, Chief
Toxicology Branch (TS-769C)
Hazard Evaluation Division

Applicant: Chevron Chemical Company
Ortho Consumer Product Division
940 Hensley Street
Richmond, CA 94804-0036

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Action Required:

Review of the toxicity data of Triox Vegetation Killer and consideration of its
signal word change are requested by the Registration Division.

RECOMMENDATIONS:

- (1) The request for change of human hazard signal word from "WARNING" to "CAUTION" is not toxicologically supported. The results of skin irritation (CC-9902) test fall in toxicity category II. Further, the core classification for acute inhalation toxicity study is "Supplementary".
- (2) Other requests for change, namely, A-dilution of the Prometon Herbicide, C-from "skin" to "eyes" and D-from "get medical attention" to "see a doctor if irritation persists" in labeling can not be approved this time because of severe toxicity of the Triox Vegetation Killer to skin.
- (3) It will be the applicant's responsibility to submit the missing data on the body weight of the individual rats and the pathological data of the organs and tissues from both treated and control animals (Acute Inhalation Toxicity Study) for further review and evaluation.
- (4) It should be noted that [redacted] is a suspected human carcinogen. The applicant is requested to explain the relationship between [redacted] be explained in details.
- (5) It should be also noted that Prometon appeared on the list of "Chemicals Potentially containing Nitrosamines" (Memo from Dr. M. Rogoff & Mr. D. Camp, 10/20/76).
- (6) In fact, the three "TRIOX VEGETATION KILLER"s, namely EPA registered I.D.#239-2381 and new formulation products: SX-1018 from CC-8354 & SX-1121 (CC-9902) are

JL

INERT INGREDIENT INFORMATION IS NOT INCLUDED

REVIEWS OF THE TOXICITY DATA ON TRIOX VEGETATION KILLER:

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I. S-1282: The Acute Oral Toxicity of Triox Vegetation Killer by G. H. Eisenlord, Z. A. Wong and J. A. MacGregor of Environmental Health & Toxicology Division of Standard Oil Company of California, 225 Bush Street, San Francisco, Calif.; SOCAL 1260/31:148; dated 9/6/78.

A. Experimental procedures stated in the report:

- (1) The Triox Vegetation Killer used in this test was supplied by the Chevron Chemical Co.. It was a clear, yellowish liquid, coded SX-1018 as stated in this application. The analytical data and its ingredients are herewith attached at the end of the reviews.
- (2) The Sprague-Dawley derived adult rats were used: Male(206 - 282 gms.); female(207 - 241 gms.).
- (3) Single intragastric doses (0, 1.5, 2.2, 3.3, 5.0, and 8.0 g/kg of the undiluted test material) were administered to groups of 5 fasted male and female rats. Five rats of each sex served as the controls. The rats were weighed prior to treatment and at 7 and 14 days after treatment.
- (4) After 14 days, the surviving animals were sacrificed and examined for gross pathological changes.
- (5) The weights of treated and control rats were compared using a Student t-test.

B. Results stated in the report:

- (1) Deaths occurred from 5-45 hrs. for males and 5-120 hrs. for females at the highest dose level of 8.0 g/kg, while 4-67 hrs. for males and 4-19 hrs. for females at dose level of 5.0 g/kg.
- (2) "Depression, diarrhea, salivation and collapse were seen within one hour after dosing" as stated in the report.
- (3) "Discharge from the eyes and nose was seen in both dying and survived rats" in accordance with report.
- (4) No gross pathological changes were seen in the organs and tissues, such as heart, lungs, liver, small and large intestines, skin, trachea and fat, etc
- (5) Most survivors gained normal weights, but two surviving males reduced weight gains in the highest dose group.
- (6) The LD50 and 95% confidence limits were 6.9^{3/4}(2.0-23.6) for males and 4.4^{3/4}(2.3-8.6) for females.

C. Conclusions

- (1) Core classification: Minimum.
- (2) Toxicity category: III for females (LD50: 4.4 g/kg).
IV for males (LD50: 6.9 g/kg).

II. S-1283: The Acute Dermal Toxicity of Triox Vegetation Killer by G. I. Rittenhouse, Z. A. Wong and J. A. MacGregor of Standard Oil Company of California; SOCAL 1261/29:96; dated 9/6/78.

A. Experimental procedures stated in the report:

- (1) The test material was also a clear yellowish liquid, coded SX-1018.
- (2) Male New Zealand white rabbits (2.30 - 2.62 kg) were used in the test.
- (3) The fur on the trunk of 5 animals was clipped the day before the testing. Three of the rabbits were abraded on the day of testing. One dose of the test material at the level of 5 g/kg was applied to the trunk of each animal.

- (4) A plastic sheet was used wrapping around the animal's trunk in order to keep the test material held in contact with the animal's skin. Six clipped, untreated rabbits were also wrapped in the same way and served as the controls.
- (5) The wrappings and any remaining material were removed from the animals after a 24-hour exposure period.
- (6) The animals were observed for 14 days and then sacrificed and examined for gross pathological changes.

B. Results stated in the report

- (1) No deaths occurred during the study, but the test material caused severe skin irritation.
- (2) Most of the treated animals have body weight ^{which} was significantly less ($p < 0.01$) than the body weight of the control animals at 7 and 14 days.
- (3) No gross pathological changes were observed that may be attributed to the treatment, except all the treated animals had dry flaky skin at autopsy.

C. Conclusions:

- (1) Core classification: Minimum
- (2) Toxicity category: III

III. The Eye Irritation Potential of CC-9902 by J. E. Levy, Z. A. Wong and J. A. MacGregor of Standard Oil Co. of California; Social 1542/39:104; dated 2/27/80.

A. Experimental procedures from the report

- (1) The CC-9902 used as the test material in this study was from the Chevron Chemical Co.. It was a clear colorless liquid, coded SX-1181. The analytical data and its ingredients are also here-with attached at the end of the reviews.
- (2) Male New Zealand white rabbits used in the study were 13-18 weeks old and from Nitabell Rabbitry, Hayward, Calif..
- (3) 0.1 ml of the test material was applied to the conjunctival sac of one eye in each of nine rabbits. The untreated eye of each animal served as the individual control. Then, three of the rabbits were further treated by rinsing the control and treated eye for one minute with distilled water 30 seconds after treatment.
- (4) All the eyes were examined and graded for ocular reaction at one hour, and at 1, 2, 3, 4 and 7 days, according to the method of Draize.

B. Results from the report

- (1) The data indicated that the treated-unwashed eyes had slight to moderate conjunctival irritation but no corneal opacity (Average score: 7.7 (6-10)) within the first hour after treatment; slight corneal opacity (greater than 1/4 - less than 1/2 area of cornea involved), slight iris, and slight to moderate conjunctival irritation (Average score: 12 (2-23)) within 24 hours after instillation of the test material; corneal opacity and slight to moderate conjunctival irritation persisted through 48 hours (Average score: 5.5 (6-14)) and reduced somewhat at 72 hours (Average score: 1.8 (0-7)). However, corneal opacity, iris and conjunctival irritation were reversible and clear in 7 days.
- (2) The treated-washed eyes had slight to moderate conjunctival irritation in the first hour after the treatment (Average score: 6.7 (6-8)) and slight conjunctival irritation in 24 hours (Average score: 2.0). All eyes appeared clear after 48 hours.

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C. Evaluation and conclusion :

- (1) Core classification: Minimum
- (2) Toxicity category: ~~III~~ (CC-9902 caused corneal opacity).

IV.S-1646:Skin irritation Potential of CC-9902 by J. T. Levy, Z.A. Wong and J. A. MacGregor of the Standard Oil Co. of California; SOCAL 1541/39:103; dated 2/11/80.

A. Experimental procedures stated in the report :

- (1) The CC-9902 used as the test material in the study was from Chevron Chemical Co. and was a clear colorless liquid, coded SX-1181.
- (2) Male New Zealand white rabbits used in the test were the same age and the same source from where the animals were purchased as those used in the preceding "eye irritation potential of CC-9902" in this application.
- (3) The fur on the backs of six animals was clipped the day before testing. 0.5 ml of CC-9902 was applied to each of two intact and two abraded sites on the back of each rabbit. The treated area was covered with a gauze patch which was secured by adhesive tape. After the 24-hour exposure period, the wrappings were removed and the skin wiped to remove the remaining test material. Irritation scores were made at 24, 48, and 72 hours and at 7 days according to the method of Draize.

B. Results appeared in the report:

- (1) According to the data presented in the report, it appeared that very slight (Score: 1), well-defined (Score: 2) and from moderate to severe (Score: 3) erythema ^{and edema} in both intact and abraded skin areas were present through 24 - 72 hours ^{after} 24-hour exposure period. Further, the over-all primary irritation score was 3.7 (Sum of the grades for erythema and edema reactions at 24 and 72 hours divided by 48)

C. Comments:

According to the method of J. H. Draze et al. (J. Pharmacol. Exptl. Therap., 82:377-390, 1944), evaluation of the skin reactions was made with various scores as the following:

<u>Erythema and eschar formation</u>	<u>Edema formation</u>
2= well-defined erythema	2=slight edema
3= moderate to severe erythema	3=moderate edema
4= severe erythema	4=severe edema

It appeared that a score of 3.7 would be severe reaction for both erythema and edema.

D. Evaluation and conclusion:

- (1) Core classification: Minimum.
- (2) Toxicity category: II (Severe irritation at 72 hours after treatment).

V. S-1286: The Acute Inhalation Toxicity of Triox Vegetation Killer by J. R. Rittenhouse, Z. A. Wong and J. A. MacGregor of the Standard Oil Co. of California; SOCAL 1264/36:4 dated 9/7/78.

A. Experimental Procedures stated in the report:

- (1) The test material used in the test was from the Chevron Chemical Co.. It was a clear yellowish liquid, coded SX-1C18.
- (2) Adult male (215-263 grams) and female (224-264 grams) Sprague-Dawley derived rats were used in this study.

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- (3) Vapor Exposure: The vapor was generated by routing air at 5 lpm and 10 psi through a warming coil and two successive gas scrubbers containing the undiluted test material. The total amount of test material generated was determined by weighing the scrubbers before and after the exposure.
- (4) Aerosol Exposure: An Ohio Ball Jet Nebulizer operating at 8.6 lpm and 50 psi was used to aerosolize the diluted test material. The total amount of material generated was determined by weighing the scrubbers before and after the exposure.
- (5) Groups of five rats of each sex were exposed for one hour to the test material which was generated by one of the afore-mentioned methods. The rats were individually restrained in glass tapered tubes, the tapered ends of which fit into openings spaced evenly along each side of a 21-liter cylindrical exposure chamber. Additionally, five rats of each sex were restrained but not exposed and served as the controls.
- (6) All animals were weighed : pre-exposure, immediately post-exposure, and 1, 7 and 14 days following exposure. After a 14-day observation period, the animals were sacrificed and examined for gross pathological changes. The organs and tissues to be examined in the study included: lungs, heart, stomach, nasal passages, trachea, bronchi, and skin, etc.
- (7) The weights of the test animals were compared to the weights of the controls using a Student t-test.

3. Results presented in the report:

- (1) Vapor Exposure: 7.6 grams of the test material were put into 300 liters of air during the one-hour exposure (Unit concentration = 25.33 mg/lit.). No deaths or signs of toxicity had been observed during the exposure or observation period. The report further claimed that no significant differences between the weights of test and control animals observed during the study. However, the report only provided the mean weight (Mean of five rats in the group) of the animals exposed either to the vapor or to an aerosol preparation of Triox Vegetation Killer.
- (2) Aerosol Exposure: 37.3 grams of the diluted test material were aerosolized in 516 liters of air during the one-hour exposure (Unit concentration=72.29 mg/lit.). Again, no deaths or signs of toxicity were observed. No significant differences between the weights of test and control rats were noted in the study. Only mean weight of the rats in the groups was reported.
- (3) A general statement was provided that no gross pathological changes were attributed to the test material in both methods of exposure.

C. Evaluation and conclusions:

- (1) Core classification: Supplementary (No individual weight-records for the rats in the study; No data or records for the pathological work performed as the report claimed).
- (2) Toxicity category: It would be ^{accurately} assigned after the individual weight-records for the rats in the study and the data or records for the pathological work performed in the study are submitted and evaluated by the applicant).

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DISCUSSIONS:

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I. Test materials

- (A) The active ingredient of Triox Vegetation Killer is Prometon with the chemical name of "2-Methoxy-4,6-bis(isopropylamino)-s-triazine". Pramitol is Reg. TM of Ciba-Geigy Corp. for Prometon Herbicide. It should be noted that Prometon appeared on the list of "Chemicals Potentially Containing Nitrosamines" (Memo from Dr. M. Rogoff & Mr. D. Campt, 10/20/76).
- (B) Triox Vegetation Killer (CC-9902) of Chevron Chemical Company, which is coded SX-1181, contains 58.5% of Tenneco 500-100, an inert in this preparation. However, Tenneco 1742 (Ref.: KVO350000, ETHYLENE, CHLORO, POLYMER, page #665 of 1979 Registry of Toxic Effects of Chemical Substances, Vol. I, published by NIOSH/U.S. - DHHHS, Sept., 1980) indicated that it is a suspected human carcinogen (Ref.: International Agency for Research on Cancer, 19:377(1979)).
- (C) Triox Vegetation Killer (CC-8354) of Chevron Chemical Company, which is coded SX-1018, contains 8.10% of Nonylphenol, also an inert of this preparation. Nonylphenol (Ref.: SM5600000, PHENOL, NONYL, page #239 of 1979 Registry of Toxic Effects of Chemical Substances, Vol. II, Sept., 1980) indicated ^{that} this substance causes severe skin irritation in rabbits at 10 mg. for 24 hours (Ref.: American Medical Association Archives of Industrial Hygiene and Occupational Medicine, 4:119 (1951)).

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2/19/84