

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

000714

DATE: February 16, 1978

SUBJECT: Conquer Liquid Vegetation Killer (Conquer LVK)
Caswell#96

EPA Reg.#100-522

FROM: Krystyna K. Locke
Toxicology Branch

TO: Robert Taylor
Product Manager #25

Action Type: Submission of 5 acute toxicity studies.

Summary

Ciba-Geigy Corporation submitted acute toxicity studies in support of the appropriate signal word, warnings and precautionary statements with regard to the herbicide formulation Conquer LVK. These studies will also be used to support future applications and reregistrations.

The label currently registered for Conquer LVK (copy attached to this evaluation) carries the signal word CAUTION. Acute toxicity studies submitted now support the signal word DANGER and associated precautionary statements (p. 4 of this submission). This formulation consists of 2.50% prometon, 1.00% pentachlorophenol, 0.12% other chlorophenols and related compounds, and 96.38% inert ingredients. It should be noted that pentachlorophenol and other phenols are on the RPAR list (OSPR Chemical Status Report, 11/1/77). It should also be noted that prometon appears on the list of "Chemicals Potentially Containing Nitrosamines" (Memos from Dr. Bogoff and Dr. Carot, 10/20/76).

Conquer LVK is a clear yellow liquid and was used as such in the studies summarized below.

Study Bio-Test**	Animals	Dose Levels	Exposure	Observation Days	LD ₅₀	TOX Category
Acute Oral	20 rats	600, 2025, 3038, 4556, 15380 mg/kg	-	14	3038† 356* mg/kg	III
Acute Dermal	8 rabbits	1350, 2000 mg/kg	24 hours	14	> 2000 mg/kg	III
Eye Irritation	3 rabbits 3 rabbits	0.1 ml 0.1 ml	30 sec.	14	-	I
Skin Irritation	6 rabbits	0.5 ml	24 hours	3	-	I
Inhalation	10 rats	3.27 mg/liter	4 hours	14	> 3.27 mg/liter	III

*Standard Deviation

**All of these studies were conducted by the Industrial Bio-Test Laboratories, Inc. and, therefore, will require "validation".

The report on the inhalation study (IBT 8562-09300) from the Industrial Bio-Test Laboratories to Ciba-Geigy Corporation is dated 8/16/76. The report on the remaining four studies (IBT 8530-09311) is dated 9/27/76. All of these studies but one, the oral toxicity study, meet the core-minimum data requirements. The oral toxicity study can be accepted as a supplementary study. Too few rats (2 males and 2 females) per dose level were used in the oral toxicity study and, therefore, the core-minimum data requirements are not met.

Conquer LVK is extremely irritating to skin and eyes (Toxicity Category I), and the label proposed by Ciba-Geigy (p. 4 of this submission) contains the appropriate signal word DANGER and other pertinent precautionary statements. Comments with regard to first aid are also included. Both the signal word and the precautionary statements are acceptable as proposed by Ciba-Geigy.

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STUDIES

1. Acute Ural Toxicity (20 rats).

Procedure

Five groups of Sprague-Dawley rats (weighing 174-254g), 2 males and 2 females per group, received single doses of Conquer LVK at the following levels (mg/kg of body weight): 600, 2025, 3038, 4556 and 15380. The observation period was 14 days. All of the animals were necropsied shortly after death or at the end of the observation period. The LD₅₀ value was calculated by the methods of Weil, Thompson, and Thompson and Weil. The test material was assigned a classification according to the procedure and Hodge.

Results

There was no mortality at the two lowest dose levels, 2 female rats died at the 3038 mg level and all of the rats died at the two highest dose levels. The deaths occurred within 1½ - 24 hours after dosing. The following symptoms were observed: hypoactivity, salivation, muscular weakness, diuresis, prostration, labored breathing and hemorrhagic rhinitis. During the 14-day observation period, male rats gained 72-112g and female rats gained 20-34g.

Necropsy on the nonsurviving animals revealed red lungs, gastroenteritis, pale kidneys, hemorrhage of the stomach lining (one rat) and pale liver (one rat). Necropsy on the surviving rats showed necrotic tissue in the stomach linings.

The LD₅₀ value (mg/kg of body weight) was 3038[±] 356 (standard deviation).

Comments

This study is acceptable as a supplementary study. Too few rats (2 males and 2 females) per dose level was used in this study and, therefore, the core-minimum data requirements are not met.

Conquer LVK falls into the Toxicity Category III, based on the reported LD₅₀ value.

2. Acute Dermal Toxicity (8 rabbits).

Procedure

Conquer LVK, 1350 mg and 2000 mg/kg of body weight, was applied to the hairless backs of rabbits (new Zealand strain, 2 males and 2 females per dose level), weighing 2.3-2.5 kg. The skin of 2 male and 2 female rabbits was abraded at the site of application. The exposure time was 24 hours and the observation time was 14 days.

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The animals were necropsied shortly after death at the end of the observation period. Experimental data were evaluated by the procedures of Weil, Thompson, Thompson and Weil, and Hodge.

Results:

Conquer LVK was severely irritating to rabbit skin, as evidence by beet-red erythema, edema and second degree burns at the site of application. Escharosis and fissuring were also present in these areas at 7 and 14 days after exposure. One female rabbit died at the 2000 mg dose level. Of the seven surviving rabbits, six gained weight (males, 0.10-0.36 kg; females 0.22-0.48 kg), whereas one animal lost weight (at the 2000 mg level).

Necropsy on the six surviving rabbits which gained weight during the observation period revealed no abnormalities. Necropsy on the rabbit which lost weight (0.72 kg) during the observation period showed enlarged gall bladder, pale kidneys and emaciation. Necropsing on the rabbit that died on the 6th day of the observation period revealed gastroenteritis.

The LD₅₀ value was greater than 2000 mg/kg of body weight.

Comments:

Based on the LD₅₀ value, Conquer LVK falls into the Toxicity Category III. This study meets the core-minimum data requirements.

3. Eye Irritation (6 rabbits).

Procedure

Conquer LVK, 0.1 ml, was placed into the conjunctival sac of the right eye of six rabbits (New Zealand strain). The eye of 3 rabbits were then left unwashed, whereas the eyes of 3 other rabbits were rinsed with water after 30 seconds of exposure. The eyes (cornea, iris, conjunctiva) of all animals were examined at one hour, and then at 1, 2, 3, 7 and 14 days, following exposure. The appearance of eyes was evaluated by the Draize procedure.

Results:

Conquer LVK was extremely irritating to the rabbit eyes, whether or not the eyes were washed after treatment with this formulation. The following symptoms were observed: corneal opacity and vascularization, and conjunctival redness, swelling and discharge. Corneal opacity (noted within the first hour after exposure) and corneal vascularization (which appeared on the 7th day after exposure) still persisted at 14 days, when the observation period was ended. At 7 days after exposure, the average irritation score was 41.3/110 and 40.3/110 for unwashed and washed eyes, respectively. At 14 days after exposure, the average irritation score was 24.9/110 and 21.7/110 for unwashed and washed eyes, respectively.

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Comments

Conquer LVK falls into the Toxicity Category I. This study satisfies the core-minimum data requirements.

4. Primary Skin Irritation (6 rabbits).

Procedure

Conquer LVK, 0.5 ml, was applied to the hairless backs of rabbits (New Zealand strain). One of the two test sites on each rabbit was abraded. The unwashed skin, both intact and abraded, was then examined for erythema and edema at 24 hours and 72 hours after exposure.

Results

Conquer LVK was extremely irritating to both intact and abraded skin. At 72 hours after exposure, 2nd degree chemical burns and desquamation were seen on 5 intact and 5 abraded sites.

The average irritation index for both treatment sites was 7.1/8.0.

Comments

Conquer LVK falls into Toxicity Category I. This study satisfies the core-minimum data requirements.

5. Acute Inhalation (10 rats).

Procedure

Five male and 5 female rats (Charles River strain) were continuously exposed to an aerosol of Conquer LVK (3270 mg/m³ of air), in an 80-liter chamber. Following the 4-hour exposure, the animals were observed for 14 days and then they were necropsied.

Results

The animals experienced hypoactivity or ruffed fur, but these symptoms disappeared within 9-18 hours after exposure. There were no deaths and no abnormalities were found at necropsy. The weight gain during the observation period was 80 g for male rats and 33 g for female rats.

Since there were no deaths at the exposure level of 3.27 mg/liter of air, the LC₅₀ value was greater than 3.27 mg/liter.

Comments

Based on the LC₅₀ value, Conquer LVK falls into the Toxicity Category III. This study can be classified as the core-minimum data.

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