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

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SEP 20 1984

MEMORANDUM

SUBJECT: Banner; EPA Reg. #100-AUR; Toxicology studies in support of registration
Caswell #: 323EE
Accession #: 248442

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

TO: Henry Jacoby
Product Manager #21
Registration Division (TS-767)

THRU: Christine F. Chaisson, Ph.D. C F Chaisson 9/4/84
Head, Review Section IV
Toxicology Branch
Hazard Evaluation Division (TS-769) WFB 9/20/84

FROM: William Dykstra, Ph.D. William Dykstra 6/15/84
Toxicology Branch
Hazard Evaluation Division (TS-769)

Recommendations:

1. The submitted studies are acceptable and support the registration.

Additional toxicology data on CGA 64 250 technical previously reviewed also support the registration. CGA 64250 is oncogenic to the liver of male mice. An estimate of oncogenic risks to applicators and persons exposed during re-entry into treated turf is required.

2. The label signal word of Danger for eye effects is correct. The precautionary labelling is correct and adequate.

Review:

1. Rabbit Eye Irritation with CGA 6420, 1.125E, FL 820180 (Stillmeadow project No. 2573-82; 4/20/82)

Test material: CGA 64250, 1.125E, FL 820180; clear, pale yellow, liquid; Banner formulation.

One group of nine NZW rabbits received 0.1 ml of actual undiluted test material in the left eye for each rabbit. The right eye was untreated and served as a control. Three of the nine treated eyes were washed with water for one minute beginning thirty seconds after treatment.

The treated eyes of all rabbits were examined and evaluated for irritation at 1, 24, 48 and 72 hours and 4, 7, 10, 13, 16, 19 and 21 days after treament. The cornea of each eye was examined with 0.2% sodium fluorecein at 1 and 24 hours. Any of the corneas which exhibited positive fluorecein were re-examined at each consecutive time until fluorecein staining of the cornea no longer occurred.

Results: One animal (male #9) was found dead on day 6. Corneal opacity was observed in seven of nine animals on the first day. Apparent invasion of the cornea by blood vessels was noted in three of the nine rabbits. This phenomenon was not reversible within 21 days.

Positive fluorecein staining did not occur in any nonwashed eye by day 7. Positive fluorecein staining did not occur in any washed eye on day 13;

Conjunctivities persisted in all rabbits for 7 to 13 days.

Conclusion: Banner formulation produced invasion of blood vessels in 3 of 9 rabbits which were not reversed in 21 days.

Toxicity Category I: Danger

Classification: Core minimum data.

2. Rabbit skin irritation with CGA 64250 1.125E FL 820180 (Stillmeadow project No. 2574-82; 4/14/82)

Test material: CGA 64250, 1.125E, FL 820180; clear, pale yellow, liquid; Banner formulation.

Six NZW rabbits were used in the study. Each rabbit had four test sites. Each rabbit received 0.5 ml of undiluted test material on two sites of the shaved skin under an impervious cuff for 24 hours. Two sites of the shaved skin sites on each rabbit were also abraded before treatment.

Observations for dermal irritations were made at 24 and 72 hours after treatment and daily for 13 days.

Results: Erythema and edema were present in both intact and abraded test sites at 24 and 72 hours and on day 12. Primary Irritation Score = 4.19 based on Draize evaluation of treated skin.

Toxicity Category III: Caution.

Classification: Core minimum data.

3. Guinea Pig Sensitization with CGA 64250 1.125E FL 820180 (Stillmeadow project no. 2575-82; 5/13/82)

Test material: Banner formulation; CGA 64250 1.125E FL 820180; clear pale yellow liquid.

Positive control: 1-chloro - 2, 4- dinitrobenzene (DNCB).

Two treatment groups of 10 male guinea pigs were used in the study. Positive control group (group I) were treated intradermally with a 0.50% W/V solution of DNCB in 0.9% saline. The test material treated group were treated intradermally with a 0.01% v/v solution of test material in 0.9% saline which was selcted from previous screening as the highest non-irritating level of test material.

The animals were treated on days 0,2,5,7,9,12,14,16,19,21 and 35 (challenge).

Scoring for erythema and edema were made at 24 and 48 hours after each treatment for each test site. A marked increase in positive skin reactions after the day 35 treatment (challenge dose) above those observed after day 0 treatment was indicative of a sensitizing reaction.

Results: The average score for erythema and edema for the positive control at day 0 was 0.0 and at day 35 was 3.4. These results demonstrate tht the test system was functional as a basis for detecting sensitization.

The test material produced a score of 0.0 for day 0 and 0.4 for day 35. These data also show that the test material produces skin sensitization at 0.01% in 0.9% saline.

Conclusion: The test material, Banner formulation, is a skin sensitizer when dosed intradermally in guinea pigs.

Classification: Core minimum data.

4. 21-day dermal toxicity study in rabbits with CGA-64250 technical (Pharmakon study No. PH 430-CG-00182; 8/30/82)

Test material: CGA - 64250 technical; Lot #FL-810858; colorless, odorless, viscois liquid.

Groups of NZW rabbits received dermal applications of test material on intact and abraded skin with an impervious cuff for 6 hours per day for five days a week for three weeks.

The dose administration is shown below as presented in the report:

Group	# of Animals	Dose mg/kg/day
I	20 (11m, 9F)	0
II	20 (11m, 9F)	3
III	20 (10m, 10F)	30
IV	20 (13m, 7F)	1000

The skin sites were observed for signs of erythema and edema at each application and scored according to the Draize method. Criteria evaluated included body weight, food consumption, ophthalmoscopic examination, hematology, clinical chemistry, and necropsy.

Selected organs were weighed and histopathology was performed.

Statistical evaluation of the data was performed.

Results: Two rabbits died during the study. One high dose female rabbit died on day 3 of treatment following diarrhea, decreased activity and decreased body tone. A male rabbit in the low dose group died on day 23, the scheduled day of necropsy. Neither death was considered compound- related.

Irritations to skin were noted in the 30 and 1000 mg/kg/day group. Diarrhea was observed in one control female, 2 males and 2 females at the low-dose and three males and one female at the mid-dose.

Diarrhea occurred up to 9 times in treated rabbits and only one time in the control.

Body weight increases for both male and female rabbits were comparable to controls.

Food consumption for all groups was decreased between the first and second week of test, but these decreases did not result in decreased body weight.

No compound-related eye lesions were noted in the study.

Skin irritation was apparent beginning at day 2 in the 30 and 1000 mg/kg/day groups and persisted for the remainder of the study.

The irritation index did not exceed 1.0 for mid-dose animals and 4.1 in the 1000 mg/kg/day group. Signs of irritation were observed beginning on day 15 in males, but not females, in the 3.0 mg/kg/day group. The highest index was 0.30 noted at day 19.

No compound-related effects in hematological findings and clinical chemistry findings were observed in the study.

Lower sodium values at 30 and 1000 mg/kg/day were present at pre-test evaluation but not at terminal evaluation, and therefore were not compound-related.

No compound-related findings were present in necropy results.

No compound-related organ weight effects were observed.

No compound-related histopathological findings were present in any tissue or organ except for the skin. There were mild to moderate skin lesions which were dose-related in treated animals in comparison to controls.

Findings of hyperkeratosis, acanthosis, mild dilation of blood vessels and nononuclear cells and/or heterophils in the proximal dermis were noted in a dose-related manner in the skin.

Conclusion: No systemic effects were noted at dosages up to 1000 mg/kg/day.

With respect to the skin, the test material induced mild dermal irritation at 3 and 30 mg/kg/day and moderate dermal irritations at 1000 mg/kg/day. No NOEL for skin lesions was established.

Classification: Core - minimum data