Atrazine / Review #8 / 5 pages / 8-25-77

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Releasable

9

DATE: August 25, 1977

SUBJECT: AAtrex 90W - Addition of Data to Files, EPA Reg. No. 100-585
Caswell #63, Shaughnessy #080803

FROM: Toxicology Branch
Registration Division

TO: Robert Taylor
Product Manager #25

THRU: O.E. Paynter, Ph.D.
Chief, Toxicology Branch

Recommendation

no action required

Review

1. Acute Oral Toxicity of Atrazine 90W - (Industrial Bio-Test, IBT #A9369, 5/25/71, submitted by Ciba-Geigy on 6/2/77)

Fifty Charles River albino rats ranging in body weight from 150-216g were divided into 5 groups of 10 animals each (5 male, 5 female) and administered 0.6, 0.9, 1.4, 2.0 and 3.0g/kg of the test material as a 10% (w/v) aqueous dilution by intubation. Following administration of the test material the rats were housed individually and observed for the succeeding 14 days for signs of toxicity and/or mortality. Initial and final bodyweights were recorded. Necropsies were performed on all animals.

Results

LD_{50}=1.6(1.2-1.9)g/kg
Toxic Signs: hypoactivity, ruffed fur, muscular weakness, prostration.
Necropsy: hemorrhages in the stomachs, pale livers, occult blood in the bladders, and hyperemic of the lungs.
Classification: Core-Minimum Data TOX CATEGORY:III
1) body weight and food consumption were not measured daily.

2. Acute Dermal Toxicity of Atrazine 90W - (Industrial Bio-Test, IBT #A9367, 5/25/71, submitted by Ciba-Geigy on 6/2/77)

Eight New Zealand albino rabbits ranging in body weight from 2.34-2.92kg were divided into 2 groups of 4 animals each (2 male, 2 female) and received skin applications of test material as an aqueous slurry at dose levels of 3.0 and 10.2g/kg to the intact skin of their shaved backs. The test material remained in contact with the skin for 24 hours under an impervious cuff. Following the 24 hours exposure the material was washed away and the animals observed for 14 days postexposure. Necropsies were performed on all animals. Initial and final body weights were recorded.

Results

LD_{50}>10.2g/kg
Toxic Signs: well defined erythema and moderate edema at 24 hrs.
Necropsy : unremarkable
Classification: Core-Minimum Data TOX CATEGORY:III
1) although the number of dose levels employed is rather scant; the results are definitive. Also "Guidelines" do not call for testing amounts in excess of 5g/kg.

3. Primary Eye Irritation of Atrazine 90W - (Industrial Bio-Test, IBT #A9369, 5/25/71, submitted by Ciba-Geigy on 6/2/77)

100mg of test material was placed into the conjunctival sac of the right eye of each of 6 rabbits, while 0.1ml of a 12.5% (w/v) aqueous dilution of the test material was similarly instilled into the right eye of an additional 6 rabbits. One, 24 and 72 hours, and 7 days following instillation, the cornea, iris and palpebral conjunctiva were examined and graded according to Draize.

Results

Undiluted: minimal conjunctival irritation at 1 hour, clearing by 24 hours.
Diluted (12.5%): minimal to moderate irritation of conjunctiva and iris at 1 and 24 hours, clearing by 72 hrs.
Classification: Core-Minimum Data TOX CATEGORY:III
1) an eye wash study was not performed.

4. Primary Dermal Irritation of Atrazine 90W - (Industrial Bio-Test, IBT #A9369, 5/25/71, submitted by Ciba-Geigy on 6/2/77)

500 mg of test material, moistened with water, was applied to one abraded and one intact skin site of 6 New Zealand albino rabbits and held in contact with the skin under an impervious cuff for 24 hours. Dermal irritation was scored at 24 and 72 hours using the method of Draize.

Results

P.I.=0.5/8.0 TOX CATEGORY:IV
Classification: Core-Minimum Data
1) readings were not made on 2 intact and 2 abraded skin sites.

5. Acute Dust Inhalation Study of Atrazine 90W - (Industrial Bio-Test, IBT #N9371, 1/28/71, submitted by Ciba-Geigy on 6/2/77)

Ten (5 female, 5 male) Charles River albino rats having an average body weight of 190g were exposed in a 70 liter Plexiglass inhalation chamber for 4 hours to a concentration of 1.3 mg/L (analytical concentration) of the test material in the form of a dust. Particle size was determined.* Following exposure the animals were returned to their cages and observed for changes in behavior and/or mortality for a period of 14 days. Initial and final body weights were recorded. Necropsies were performed on all animals.

Results

LC_{50}>1.3 mg/L{no deaths occurred over a 4 hour exposure period}
Toxic Signs: none
Necropsy: unremarkable
Classification: Supplementary Data TOX CATEGORY:II
1) an insufficient number of dose levels were employed; therefore, the LC_{50} could not be calculated.

*51% of the particles were in the respirable range

6. 5-Day Subacute Dermal Toxicity Study with Atr zine 90W -(Industrial Bio-Test, IBT #A9370, 5/10/71, submitted by Ciba-Geigy on 6/2/77)

Sixteen New Zealand albino rabbits ranging in body weight from 2.6 to 3.1 kg were divided into 4 groups of 4 animals (2 male, 2 female) and received skin applications of test material as a 50% aqueous dilution at dose levels of 0,250,500 and 1000 mg/kg (Atr zine 90W) once a day for 5 consecutive days. The material was applied to the shaved backs of each rabbit and allowed to remain in contact with the skin for a period of 18 hrs/application. One half of the animals were further prepared by abrading their skin prior to application of the test material. At the end of the contact period the material was washed from the skin. Each rabbit was fitted with a flexible plaster collar to prevent oral injection. Observations for mortality and abnormal behavioral reactions were made daily. Body weights were recorded initially and at termination of the experiment. At termination of the experiment, animals were sacrificed via air embolism into the marginal ear vein and subjected to gross pathological examination. The following organs were weighed:

Brain	Liver	Kidneys
Spleen	Heart	Gonads
Thyroid Gland	Adrenal Glands	

Representatives samples of liver, kidneys and skin were examined microscopically. The following tissues were preserved for possible histapathologic examination:

Adrenal Glands	Kidneys	Pituitary Gland
Aorta	Liver	Prostate Gland
Brain	Lungs	Salivary Glands
Caecum	Lymph Nodes (mediastinal and mesenteric)	Seminal Vesicle
Colon	Pancreas	Skeletal Muscle (thigh)
Esophagus	Parathyroid Glands	Skin from the Application Site
Gall Bladder	Peripheral Nerves (sciatic and femoral)	Spleen
Gonads		Sternum
Heart		

Small Intestine (duodenum, jejunum, and ileum)	Stomach	Thyroid Gland
Uteri	Trachea	Urinary Bladder

Results

No deaths or untoward behavioral reactions were noted. The 50% aqueous dilution of Atrazine 90W was mildly irritating to the skin, regardless of the amount applied. Superficial eschar formation was present along the abrasions. There was a dose related body weight loss which could be attributed to treatment. Necropsy did not reveal any significant gross pathologic alterations other than in the skin at the site of contact of the 50% aqueous dilution of Atrazine 90W. Of the tissues examined microscopically only the skin exhibited treatment related changes characterized by a mild acanthosis. One female rabbit treated at 500 mg/kg and one male treated at 1000 mg/kg had increased kidney/body-weight ratios. Upon microscopic examination the kidneys of these 2 rabbits exhibited interstitial nephritis and focal glomerulonephrites. This was considered to be a spontaneous disease not unusual for the rabbit, since one control rabbit exhibited similar pathology.

Classification: Supplementary Data

1) the duration of testing was not sufficient;
2) a larger number of tissues should have been microscopically examined; and
3) hematology and clinical chemistry parameters were not measured.

William Greear
William Greear