Atrazine/Review #9/8.29.77/7 pages

b

Releasable

August 29, 1977

AAtrex 80W - Addition of Data to Files, EPA Reg. No. 100-439
Caswell #63, Shaughnessy #080803

Toxicology Branch
Registration Division

Robert Taylor
Product Manager #25

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

Recommendation

The acute oral LD_{50}, dermal LD_{50}, eye and skin irritation toxicity studies are adequate and may be used for registration purposes. The 21-Day Subacute Dermal Study is invalid until errors in the histapathology report have been corrected (see review). Also, the registrant should comment on the natural incidence of cellular degeneration of the bone marrow in New Zealand albino rabbits.

Review

1. Acute Oral Toxicity of Atrazine 80W - (Industrial Bio-Test, IBT #?, 6/4/65, submitted by Ciba-Geigy on 6/2/77, Acc. #230305)

   Twenty male Sprague-Dawley albino rats having an average body weight of 160g were divided into 4 groups of 5 animals each and administered 3.0, 4.6, 6.8 or 10.2 g/kg of the test material as a 50% (w/v) aq. dilution by gavage. 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. Necropsies were performed on all animals which died during the experiment.

Results

LD_{50}=5.1$\pm$ 0.4 g/kg
Toxic Signs: hypoactivity, ptosis, ruffled fur, muscular weakness, dyspnea.
Necropsy: unremarkable
Classification: Core-Minimum Data TOX CATEGORY:III
1/ body weight and food consumption were not measured daily.

2. Acute Dermal Toxicity of Atrazine 80W - (Industrial Bio-Test, IBT #?, 6/4/65, submitted by Ciba-Geigy on 6/2/77, Acc #230305)

Sixteen New Zealand albino rabbits having an average weight of 2.5 kg were divided into 4 groups of 4 animals each (2 male, 2 female) and received skin applications of 4.6, 6.8, 10.2 or 15.4 g/kg of the test material as a 75%(w/v) aq. suspension to the intact skin of their shaved backs. The test material remained in contact with the skin for 24 hrs. under an impervious cuff. Observations for mortality local reactions, and behaviorialaabnormalities were continued for a period of 14 days following the skin applications. Necropsies were performed on animals that died during the experiment.

Results

LD_{50}=9.3 ± 0.9 g/kg
Toxic Signs: lethargy, emaciation, tremors, salivation, paralysis of the fore and hind limbs (permanent), slight to mild eythemene and edema of skin at treatment sites.
Necropsy: unremarkable
Classification: Core-Minimum Data TOX CATEGORY:III
1) body weight and food consumption were not measured daily.

3. Primary Eye Irritation of Atrazine 80W - (Industrial Bio-Test, IBT #?, 6/4/65, submitted by Ciba-Geigy on 6/2/77, Acc #230305)

50 mg of test material was placed into the conjunctival sac of the right eye of each of 5 rabbits. One, 24, 48 72, 96 hrs. and 7 days following instillation, the cornea, iris, and palpebral conjunctiva were examined and graded according to Draize.

Results

Corneal opacity was present in 2/5 rabbits at 1 hr., clearing by 24 hrs. All rabbits exhibited minimal irritation of the iris and conjunctiva which cleared by 72 hrs.

Classification: Core-Minimum Data TOX CATEGORY:II

1) an eye wash study was not performed
2) although only 5 animals were tested, the results are similar between animals thus giving credence to the results.

4. Primary Dermal Irritation of Atrazine 80W - (Industrial Bio-Test, IBT #?, 6/4/65, submitted by Ciba-Geigy on 6/2/77, Acc #230305)

500 mg of test material, moistened with water, was applied to one abraded and one intact skin site on each of 4 albino rabbits and held in contact with the skin for 24 hrs. Dermal irritation was scored at 24 and 72 hrs. by the method of Draize.

Results

P.I.=0.5/8.0 TOX CATEGORY·IV

Classification: Core-Minimum Data

1) although only 4 animals were used the results are uniform thus giving credence to the results.

5. Acute Inhalation Toxicity of Diazinon 25W, Chlorobenzilate 25W, Methoxy chlor 50, DDT-BA 75, Simazine 80W, Atrazine 80W and Propazine 80W - (Woodard Research Corp. Report #?, 3/16/62, submitted by Ciba-Geigy on 6/2/77, Acc #230305)

Groups of animals were exposed for 1 hr to dust of various test materials. The dust was introduced into the cylind body of the exposure chamber by a Wright Dust Feed Mechanism. Analyses of dust concentration in the chamber were performed gravimetrically. Animals were observed for behaviorial abnormalities and/or mortality for 14 days postexposure. Listed below are chamber concentration, mean weights of test animals, and total number of animals exposed to each compound.

Compound	Concentration mg/liter	Mean Wt in Grams of Test Animals	No of Animals Exposed
Diazinon 25 W	2.1	192	10
Chlorobenzilate 25 W	2.5	139	10
Methoxychlor 50	2.6	183	9
DDT-BA 75	4.9	180	10
Simazine 80 W	1.8	201	9
Atrazine 80 W	2.0	200	8
Propazine 80 W	3.3	213	10

Necropsies were not performed.

Results

No deaths or signs of toxicological or pharmacological effects due to exposure were noted in any case. Twenty-four hours after exposure all animals appeared in normal condition. The test animals were subjected to gross autopsy 14 days after exposure. One animal, Simazine 80 W - male, showed minor abnormalities in the lung and enlarged lymph nodes in the area of the thymus. All other animals were noted as normal. Weight gains were within normal limits. LC_{50} values would necessarily exceed the values reported as air concentrations for each chemical, respectively.

Classification: Core-Minimum Data TOX CATEGORY:III
1) although only 1 dose level was tested, it was tested at the highest concentration that could be generated.

6. 21-Day Subacute Dermal Toxicity of Atrazine 80W - (Industrial Bio-Test, IBT #?, 6/4/65, submitted by Ciba-Geigy on 6/2/77, Acc #230305)

Fifty New Zealand albino rabbits weighing 2-3 kg were divided into 5 groups of 10 animals each (5 male, 5 female). Group designations were as follows:

Group	Condition of Skin	Dose (g/kg/day)	Number of Applications
Control	intact	-	15
T-I	intact	1.0	15
T-II	abraded	1.0	15
T-III	intact	2.0	15
T-IV	abraded	2.0	15

Following application, the test material was allowed to remain in contact with the skin for 7 hours/day, 5 days/wk for 3 weeks. At the end of each contact period the body coverings were removed and the test material washed from the skin. Checks for mortality and abnormal behaviorial reactions were made daily. The following test parameters were measured initially and at termination of the experiment:

Hematology

Hb
PCV
RBC
WBC
Differential WBC

Clinical Chemistry

BUN
SAP

Urine Analyses

Reducing Substances
pH
Albumin
Microscopic Elements

At termination of the experiment, animals were sacrificed and necropsied. The following organ weights were obtained:

Liver
Heart
Thyroid Gland
Kidneys
Brain
Adrenal Glands
Spleen
Gonads

The following tissues were prepared for histological examination:

Heart
Lungs
Pancreas
Small Intestine (duodenum, jejunum, ileum, caecum)
Kidneys
Prostate
Pituitary
Thyroid Gland
Skeletal Muscle (thigh)
Brain
Aorta
Liver
Esophagus
Colon
Spleen
Urinary Bladder
Seminal Vesicles
Adrenal Glands
Parathyroid Glands
Sternum
Skin (from application site)
Trachea
Gall Bladder
Stomach
Lymph Nodes (mediastinal, mesenteric)
Gonads
Uterus
Salivary Glands
Peripheral Nerves (sciatic, femoral)

Results

Animals receiving applications of the test material exhibited weight loss and appeared listless after the 3rd application. Only animals in the high dose group displayed partial paralysis of the entire body after 3 applications. These animals exhibited salivation and complete paralysis in 1/2 of the animals after 12 applications. Slight erythema was noted after 3 applications of the test material, followed by cracking and degeneration after 6-8 applications. Mortality (20-50%) occurred in all test groups and appeared to be unrelated to dose applied or to condition of the skin (intact vs. abraded). Hematology, clinical chemistry and urinalyses values were comparable between test and control animals. The brain/body weight ratio was increased in test animals, which is probably no more than a reflection of adecrease in body weight. The histopathological evaluation can not be assessed at this time due to errors in reporting, i.e. it is doubtful that pericholangitis was actually observed in the lung of 2 male rabbits.

Classification: Invalid
1) due to errors in reporting the study must be considered invalid until the errors have been corrected.

Further, since bone marrow degeneration was observed in some of the control and test animals, an attempt should be made to determine the natural incidence of bone marrow degeneration in animals of this strain.

William Greear