1-17-95

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

JAN 17 1995

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011388

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Atrazine, Dermal Absorption in Rats

TO: Walter Waldrop PM 71
Reregistration Branch
Special Review and Reregistration Division (7508C)

1/6/95

FROM: Robert P. Zendzian Ph.D.
Senior Pharmacologist
Toxicology Branch I
Health Effects Division (7509C)

THROUGH: Karl Baetcke Ph.D.
Chief
Toxicology Branch I
Health Effects Division (7509C)

1/6/95

Compound; Amatraz Tox Chem #063 ID #; 080803

Registrant; Ciba-Geigy MRID 433143-02 DP Barcode; D206233

Action Requested

Review the following study;

Study Type Dermal Absorption (85-3)

Citation
A dermal radiotracer absorption study in rats with ^{14}CAtrazine. C.P. Chengelis. WIL Reseaech Laboratories. WIL Study no 82048. June 22, 1994. MRID 433143-02.

Core Classification Acceptable

Conclusions
4 Male rats per dose and duration dosed at 0.01, 0.1 or 1 mg/cm^2. 0.5, 1, 2, 4, 10 and 24 hours exposure and 10 hours exposure, washed, to 34, 58 and 82 hours and 24 hours exposure, washed, to 48, 72 and 96 hours. Percent absorbed increased with time decreased with dose. Significant portion of dose remaining on washed skin with subsiquent absorbption. See DER for detailed data.

Effects of this new data, if any, on the atrazine risk assessent will be considered separately.

Attachment DER

1 of 8

Data Evaluation Report

011382

Compound Atrazine

Study Type Dermal Absorption (85-3)

Citation

A dermal radiotracer absorption study in rats with ^{14}C-Atrazine. C.P. Chengelis. WIL Reseaech Laboratories. WIL Study no 82048. June 22, 1994. MRID 433143-02.

11/1/94

Reviewed by Robert P. Zendzian PhD
Senior Pharmacologist

Core Classification Acceptable

Conclusions

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Materials

Atrazine. ^{14}-C
vial 1, CL-XXII-45
specific activity 1.9 uCi/mg
radio purity 98.7%
vial 2 & 3, CL-XXII-47
specific activity 19.1 uCi/mg
radio purity 98.9%
from Geigy

4L blank No FL 901240
Reference 82047-3

Male Charles River CD rats 30-32 days of age
from Charles River Portage Michigan

Experimental Design

Four rats per dose and exposure duration were dosed at 0.1, 1 or 10 mg/rat according to the dosing schedule given below. The application site was washed at 10 or 24 hours on the animals designated as exposed for 10 or 24 hours and subsiquently terminated at 34 to 96 hours.

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Exposure Duration (hours)	Termination (hours)
0.5	0.5
1	1
2	2
4	4
10	10
24	24
10	34
10	58
10	82
24	48
24	72
24	96

Dose preportration

"For the low dose formulation 10.4 mg of blank 4L formulant was added to Vial No 2 (containing ^{14}C-Atrazine) followed by the addition of 4.0 ml of deionized water." The materal was mixed, sonicated and maintained on a magnetic stirring plate.

"For the mid dose formulation 104 mg of blank 4L formulant was added to Vial No 3 (containing ^{14}C-Atrazine) followed by the addition of 4.0 ml of deionized water," The materal was mixed, sonicated and maintained on a magnetic stirring plate.

"For the high dose formulation 1.04 gm of blank 4L formulant was added to Vial No 1 (containing ^{14}C-Atrazine) followed by the addition of 8.0 ml of deionized water." The materal was mixed, sonicated and maintained on a magnetic stirring plate.

All dosing suspensions were analyzed on the day of preparation and on each day of dosing before administration. Radiochemical purity was determined for each dosing suspension.

Application of test material

The back of each rat was shaved 24 hour prior to dosing and the shaved area washed with acetone. "Before application of the test material, a small linked stainless steel jewelers chain waas attached to shackle the rear legs of each rat to prevent scratching of the treated area. The skin of the dose area was defined and enclosed with a nonocclusive covering or "protective appliance", which consisted of a piece of Stomato-ahesive, filter paper and an aluminum bridge. The Stomahesive was affixed to the skin with Skin-Bond® cement to form a "well" surrounding the area of skin to be treated.

The treated area was covered with filter paper elevated by a foil bridge to prevent contact with the applied dose. The application site, within the "well", was a 10.0 cm^2 area (2.5 cm X 4.0 cm)."

Test material was applied with a positive displacement pipette and spread with the tip. The pipette was washed with ethanol to determine residual material. Actual dose applied was determined by subtraction. The rat was placed in a Nalgene metabolism unit and urine and feces collected separately for the entire exposure period.

At the end of the exposure period, the filter paper and foil bridge was removed and the application site washed with Liquid Dove in water and rinsed with water. Animals scheduled for termination at 0.5 to 24 hours were euthanized with CO^2. The abdominal cavity was opened and a 5 to 7 ml sample of blood taken from the inferior vena cava. The Stomatohesive was removed and the application site skin and the skin under the Stomatohesive were collected separately. Residual bladder urine was collected and added to the last urine collection. The residual carcass was collected.

Animals schedured to be terminated beyond 24 hours were returned to the origional metabolism unit. At termination these rats were again washed and terminated as above.

Samples analyzed were as follows:

Application device wash
Skin wash
Application site skin
Blood
Urine
Feces
Carcass

Results

Blood concentrations are presented in Table 3 and dose distribution in Tables 4, 5 and 6 from the report.

TH Review 011388

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