11-21-85

PB-1061
TXR-4102

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 004802
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: EPA ID Number: 061601; EPA Registration No. 239-2486
Paraquat: Evaluation of 21-Day Dermal Toxicity Study in Albino Rabbits.

Accession No. 259878 Tox. Chem. No. 634
Record No. 162291 Project No. 835

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11-15-85

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11/21/85

Toxicology Branch/HED has completed an evaluation of the following study:

1. Paraquat: 21-Day Dermal Toxicity Study in Albino Rabbits. Hazleton Laboratories America, Inc.; Report No. 2107-132; October 25, 1985

The submitted report is an "Unaudited Draft." It was submitted prior to completion of the histopathology section, and it was not reviewed for GLP compliance. This report was submitted, "...as justification of our good faith efforts in meeting the Paraquat Data Call-In and extension request..." A complete report will be submitted in the future. Based on the unaudited draft, this study was classified as Core Supplementary.

There were few indications of compound-related toxicity at the doses tested. The NOEL was defined as 1.15 mg cation/kg/day. The LEL was defined as 2.60 mg cation/kg/day at which dose there was dosing site scabbing. At the 6.00 mg cation/kg/day dose, there was slight to well-defined erythema and scabbing which began on day 11 and persisted and worsening during the study. The males at this dose also had reduced absolute and relative testicle weights of 17-22%.

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Study Type: Subacute Dermal Toxicity

Study Title: Paraquat: 21-Day Dermal Toxicity Study in Albino Rabbits; Report No. 2107-132.

Accession No.: 259878

Record No.: 162291

Sponsor: Chevron Chemical Company
Richmond, California

Testing Laboratory: Hazleton Laboratories America, Inc.
Vienna, Virginia

Test Material: Paraquat Technical (SX-1465)
[NOT OTHERWISE SPECIFIED]

Date of Final Report: October 25, 1985

PROTOCOL:

Randomized groups of six male and six female New Zealand White rabbits were dermally dosed with Paraquat for 6 hours/day over 21 consecutive days at cation dose levels of 0 (control), 0.5, 1.15, 2.60, and 6.00 mg/kg/day (nominal Paraquat doses of 0, 1.5, 3.4, 7.8, and 17.9 mg/kg). They were observed twice daily for clinical signs, and weekly for food consumption. Dermal irritation was graded prior to dosing and on days 1, 2, 4, 8, 11, 15, 18, and 21. Body weights were measured on days -7, -4, 1, 4, 8, 11, 15, and 18. The following clinical pathology parameters were measured prior to dosing (day -6) and at study termination (day 22):

Hematology

Erythrocytes	Platelets
Reticulocytes	Leukocytes
Hemoglobin	Differential leukocytes
Hematocrit	

Clinical Chemistry

Bilirubin, total	Alkaline phosphatase
Bilirubin, direct	CK [sic]
BUN	LDH
Creatinine	Triglycerides
Total protein	UAC [sic]
Albumin	Sodium
Globulin	Potassium
Glucose	Chloride
AST	Calcium
ALT	Phosphorus
Total cholesterol	

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At the termination of the study, all rabbits were necropsied and the following organs were examined (weights were measured for asterisked organs):

*Brain	*Ovaries
*Adrenals	Treated skin
*Lungs	Untreated skin
Heart	Adipose tissue
Spleen	Bones (not otherwise specified)
*Liver (with gallbladder)	Stomach
*Kidneys	Colon
*Testes	

RESULTS:

There were no findings of erythema or edema in any rabbits at the 2.60 mg cation/kg/day dose, but scabbing was seen in two males (days 18 and 21) and 1 female (days 15, 18, and 21). The rabbits dosed at 6.00 mg cation/kg/day had very slight to well-defined erythema and scabbing beginning on day 11 and persisting and worsening during the study.

No clinical signs of toxicity were reported during the course of the study at any dose. Body weights and food consumption were similar for all groups throughout the study. There were no indications of compound-related clinical pathology anomalies. The only dose-related gross lesions were skin lesions at the treated skin sites. These included scabs at the 2.60 and 6.00 mg cation/kg/day dose, and redness, thickening and prominent subcutaneous vessels at the 6.00 mg cation/kg/day dose. Absolute and relative organ weights were similar for all groups, except for testicle weights which were reduced 18% for absolute weights and 17% to 22% for testes to body weight and testes to brain weight ratios in the 6.00 mg cation/kg/day group. The significance of this finding is uncertain in the absence of individual animal histopathologic and organ weight data.

NOEL = 1.15 mg cation/kg/day
LEL = 2.60 mg cation/kg/day (dosing site scabbing without other evidence of irritation)

Core Classification: SUPPLEMENTARY. Because of the inherent deficiencies in this "Unaudited Draft," this study cannot be acceptable until all data is submitted. The study is lacking an acceptable textual presentation of the study design, results, discussion, and conclusion. It is lacking specifics on dosing procedure, such as whether the skin was abraded or occluded. The age and weight range of the rabbits, and the purity and formulation of the test article were not given. Since there was no mention of the formulation, it was impossible to determine whether the control rabbits were untreated or treated with an unspecified vehicle. The clinical chemistry parameters CK and UAC were not defined, and therefore cannot be interpreted. The final report will contain the histopathology results, and will then be suitable for Quality Assurance review.

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