

US EPA ARCHIVE DOCUMENT

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

003828

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Chevron's comments on Toxicology Branch evaluation of human dermal absorption studies with paraquat.

Tox. Chem. No.: 634

TO: Robert Taylor/V. Walters
Product Manager, Team #25
Registration Division (TS-769)

FROM: Krystyna K. Locke, Toxicologist
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769) *Krystyna K. Locke 5/10/84*

THRU: Albin B. Kocialski, Acting Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769) *ABK 5/13/84*

THRU: William L. Burnam, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769) *WLB 5/13/84*

On March 29, 1983, Toxicology Branch/HED completed an evaluation of the following submission: "Human Percutaneous Absorption of Paraquat", EPA Accession No. 249511, EPA Record No. 91977.

That submission consisted of 4 individual studies: one study with Rhesus monkeys in which urinary excretion of the injected (i.m.) ¹⁴C-paraquat dichloride was studied; and three studies with adult human males in which the dermal absorption of ¹⁴C-paraquat dichloride was investigated. The study with monkeys was evaluated separately by Toxicology Branch/HED. Because the only difference in conducting of the three dermal absorption studies was an application site, these studies were evaluated together.

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Due to insufficient experimental details, each study was classified as Acceptable as Supplementary. There are no core criteria for these types of studies.

The current submission (EPA Record No. 114047; copy attached) contains the missing experimental details and the above-mentioned studies are, therefore, reclassified as Acceptable.

Attachment

- TS-769:th:TOX/HED:KILlocke:5-11-84:card misc.437



Ortho

Chevron Chemical Company
940 Hensley Street, Richmond, CA 94804

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September 15, 1983

Research and Development
Agricultural Chemicals Division

Faraquat: Rhesus Monkey and Human
Percutaneous Absorption Studies.
Your Letter Dated May 9, 1983.
EPA Accession Number 249511.

Mr. Robert J. Taylor (PM-25)
Registration Division (TS-767)
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. Taylor:

We received your comments, dated May 9, 1983, on the subject studies and our response is attached.

We trust that this response will satisfactorily answer the questions you raised on these studies.

Our records show that the one Accession Number, 249511, was assigned to the Rhesus Monkey and the Human studies. Please confirm that this is correct.

Yours sincerely,

L. R. Stelzer, Manager
Registration & Regulatory Affairs

HDB:sag/D2-11

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Chevron Environmental Health Center, Inc.

003828

August 25, 1983

RESPONSE TO THE U.S. ENVIRONMENTAL PROTECTION AGENCY LETTER OF MAY 9, 1983
REGARDING PARAQUAT RHESUS MONKEY STUDY AND PARAQUAT HUMAN ACUTE DERMAL
ABSORPTION STUDY.

Please refer to the attached letter (R. J. Taylor to L. R. Stelzer) for the questions/comments being addressed.

RHESUS MONKEY STUDY

1a. The radiopurity of the test material was 99.8%.

The radiolabeling on the Paraquat molecule was on the methyl groups i.e., [¹⁴C-methyl] paraquat dichloride.

Animals were housed singly in suspended, stainless steel cages at the Primate Center of the University of California, Davis. They were fed standard monkey chow supplemented with fruit. Tap water was available ad libitum.

Twenty-four hour urine samples were collected daily. Samples were stored frozen until analysis.

1b. We agree with your calculations that a 0.25 ml dose contained 6.44 μ Ci of paraquat dichloride and not the 4.72 μ Ci reported by the author. Please note that the concentration stated in your paragraph should be 2.4 mg of paraquat ion/ml (and not 2.4 μ g of paraquat ion/ml).

HUMAN ACUTE DERMAL ABSORPTION STUDIES

1. In addition to your comment, please note that these studies should be evaluated together since data from the monkey experiment were used as a basis for human urinary excretion to obtain the values for the percutaneous absorption data.

2a. Please refer to our answer to 1a.

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2b,c. The human subjects were paid community volunteers. Individual identification and age are as follow:

		<u>Age</u>
Subject #1	(R.H.)	33
Subject #2	(J.R.)	41
Subject #3	(R.S.)	30
Subject #4	(R.M.)	49
Subject #5	(C.B.)	74
Subject #6	(J.L.)	39

- 2d. The subjects lived at home during the test period.
- 2e. Urine samples were brought to the laboratory for analysis every 24 hours. For each time period, total urine volume was measured and a 20 ml aliquot was removed and stored frozen until assayed.
- 2f. Application sites were covered only by the volunteer's clothing. There was no specific occlusion.
- 3. As previously stated in 1b above, we agree with your calculations. Since the stock solution contained 2.4 mg of paraquat ion/ml, each application contained 11.83 μg of paraquat dichloride/cm².

Please note that this small calculation error (11.83 $\mu\text{g}/\text{cm}^2$ instead of 9 $\mu\text{g}/\text{cm}^2$ as reported) resulted from the author's use of the molecular weight of paraquat dichloride rather than paraquat cation. This calculation error in no way changes the conclusions reached by the author that the test material was absorbed very poorly (less than 0.3% of the applied dose).