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

JUN - 4 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

007965

SUBJECT: Malathion---Toxicology
Data Submitted under MRID 41451201
EPA ID # 57875

Chemical (Caswell) 535
RD Record No. 263,284
HED Project 0-1142Z

FROM: Irving Mauer, Ph.D., Geneticist
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5-18-90

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THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I (IRS)
Health Effects Division (H7509C)

5/26/90

Registrant: American Cyanamid, Princeton NJ, on behalf of the Malathion Reregistration Task Force (No. 57875), in conjunction with A/S Cheminova.

Request: Review and evaluate the following mutagenicity study: Acute Test for Chemical Induction of Chromosome Aberration in Rat Bone Marrow Cells In Vivo with AC 6,601, performed by SITEK Research Labs., Rockville MD, Study # 0125-1531, Final Report Dated January 10, 1990 (EPA MRID 41451201).

TB Conclusion: ACCEPTABLE

The study reported negative results for inducing chromosome aberrations in rat bone marrow cells at toxic doses (up to 2000 mg/kg).

ATTACHMENT (DER)

Printed on Recycled Paper

Reviewed by: Irving Mauer, Ph.D., Geneticist, 5-18-90
Toxicology Branch I (IRS)/HED
Secondary reviewer: Karl P. Baetcke, Ph.D., Chief 5/26/90
Toxicology Branch I (IRS)/HED

DATA EVALUATION RECORD

I. SUMMARY

MRID (ACC) 41451201
ID No. 57875
RD Record 263,284

CASWELL 535
Project 0-11427

STUDY TYPE: (84-2) Mutagenicity --- chromosome damage in vivo (Rat BM)

CHEMICAL: Malathion

SYNONYMS: AC 6,601

SPONSOR: American Cyanamid, Princeton NJ (and A/S Cheminova).

TESTING FACILITY: SITEK Research, Rockville MD

TITLE OF REPORT: Acute Test for Chemical Induction of Chromosome Aberrations in Rat Bone Marrow Cells In Vivo with AC 6,601

AUTHORS: Ramadevi Gudi

STUDY NUMBER: 0125-1531

DATE OF ISSUE: January 10, 1990

TB CONCLUSIONS:

Negative for inducing chromosome aberrations in bone marrow cells of male and female Sprague-Dawley rats gavaged acutely at doses up to clinically toxic and cytotoxic levels (2000 mg/kg).

CLASSIFICATION (CORE-GRADE):

ACCEPTABLE

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DETAILED REVIEW

A. Test Material: AC 6,601 (Malathion, American Cyanamid)
Description: Clear, pale-yellow liquid
Batch (Lot): AC 6015-136B
Purity (%): 94.0
Solvent/carrier/diluent: Corn oil

B. Test Organism: Rodent
Species: Rat
Strain: Sprague-Dawley
Age: 6 wk
Weights - males: 218-236g
females: 161-179g
Source: Charles River, Raleigh, NC

C. Study Design (Protocol): This study was designed to assess the clastogenic potential of AC 6,601 when administered once by oral gavage to Sprague-Dawley rats, according to standardized (referenced) procedures.

A statement affirming compliance with Agency GLPswas provided.

A statement of Quality Assurance measures (inspections/audits) was also provided.

D. Procedures/Methods of Analysis: Following a dose-selection test (6 doses ranging from 1.25 to 6250 mg/kg), groups of 5 males and 5 females were gavaged once with 0 (corn oil vehicle), 500, 1000 and 2000 mg/kg test article, and sacrificed 12, 24 and 48 hours later. A final group of rats (5 male: 5 female) was injected i.p. with the mutagen triethylenemelamine (TEM, 0.5 mg/kg) as positive control, and sacrificed 24 hours later.

Approximately 2-3 hours before sacrifice, each animal was injected with the mitotic-arresting agent, colchicine (1 mg/kg). Femoral bone marrow cells were removed at scheduled sacrifice and processed by standard cytological procedures into microscope slide preparations of metaphases.

Fifty metaphases per animal were scored on coded slides (250 per sex per treatment group) for the conventional assay of structural chromosome aberrations and polyploidy; as well, 500 cells per animal were scanned for mitotic index (no. metaphases per 500 x 100).

Aberration data were analyzed by Chi-square, with p set at ≤ 0.05. Criteria employed by expert practitioners of this assay for both assay acceptance and responses were presented.

E. Results: In the range-finding test, the test substance was lethal to animals within 24 hours of treatment with 3125 and 6250 mg/kg, but survivors (given 1250 mg/kg and less) showed no clinical signs or body weight changes, and mitotic indices were comparable to vehicle control (Report Tables 1 and 2). Therefore, 2000 mg/kg was chosen as the highest dose to be tested in the main assay, and two lower doses, 1000 and 500 mg/kg (delivered as 1.6, 0.8 and 0.4 ml/kg, since test substance density = 1.25).

Although no overt clinical signs were observed in any test animal, high-dose males (2000 mg/kg) gained less weight and/or lost weight post-treatment (Report Table 3), and mitotic indices decreased in a dose responsive fashion 24 hours after treatment (Report Table 4). However, despite these toxic changes, no significant increases over solvent control in aberrations were recorded in any treatment group, in contrast to the positive control (TEM) which responded as expected.

The author concluded that AC 6,601 was not clastogenic under the conditions of this assay.

F. TB Evaluation: Acceptable.

This study was performed with adequate procedures and appropriate controls such as to render the negative result valid.

Attachments (Data Tables)

RIN 1244-00

Malathion Tox Review # 7965

Page_____ is not included in this copy.

Pages 5 through 7 are not included.

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_____ Identity of product inert ingredients.

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