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

008504

AUG 9 1991

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OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Sodium chlorate - Tox. Data Submitted under MRID Nos. 412562-01, -02, -03, -04, -05, and -06, in Support of a Section 18 Emergency Exemption ID No. 91TX0022

Chemical (Caswell) No.: 753
RD Record No.: S-396696
HED Project No.: 1-1718

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Irving Mauer 7/26/91

TO: Rebecca Cool/Susan Stanton, PM Team 41
Registration Support Branch
Registration Division (H7505C)

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

Karl P. Baetcke 8/5/91

Registrant: Kerr McGee Chemical, Oklahoma City (OK), agent for the Sodium Chlorate Task Force (SCTF)

Request

A. Review and evaluate the following five (5) mutagenicity studies, all performed for the registrant in the laboratories of the Life Science Research Ltd. facility of the Roma Toxicology Center SPA (LSR-RTC):

1. Sodium Chlorate: Assessment of Mutagenic Potential in Histidine Auxotrophs of Salmonella typhimurium (The Ames Test), LSR-RTC Report No. 89/SKR001/0285, dated August 14, 1989 (MRID No. 412562-01).

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2. Sodium Chlorate: Investigation of Mutagenic Activity at the HGPRT Locus in a Chinese Hamster V79 Cell Mutation System, LSR-RTC Report No. 89/SKR002/0631, dated September 18, 1989. (MRID No. 412562-02).

3. Sodium Chlorate: Assessment of Clastogenic Action on Bone Marrow Erythrocytes in the Micronucleus Test, LSR-RTC Report No. 89/SKR003/0253, dated August 25, 1989 (MRID No. 412562-03).

4. Sodium Chlorate: Assessment of Its Ability to Cause Lethal DNA Damage in Strains of Escherichia coli: LSR-RTC Report No. 89/SKR004/0341, dated September 5, 1989 (MRID No. 412562-04).

5. Unscheduled DNA Synthesis (UDS) in HeLa S3 Cells In Vitro, LSR-RTC Report No. 102002-M-02289, dated September 27, 1989 (MRID No. 412562-05).

B. Appraise the interpretation of these genotoxicity studies submitted by Ben-Dyke Associates, Inc., Whitehouse Station, NJ (the registrant's toxicology consultant) dated September 29, 1989.

TB Conclusions:

A. The five submitter studies have been judged as follows (detailed reviews are appended to this cover):

Study No./Type (MRID)	Reported Results	TB Evaluation
(1) 89/SKR001/0285 Ames Test (412562-01)	Negative up to limit dose (5000 ug/plate), with/without metabolic activation.	Acceptable
(2) 89/SKR002/0631 V79/HGPRT (412562-02)	Negative for inducing gene mutation in V79 cells in vitro, exposed with/without activation up to 5000 ug/mL.	Acceptable
(3) 89/SKR003/0253 Mouse MT (412562-03)	Negative for inducing chromosome damage in PCE (micronuclei) in mice treated orally once up to 5000 mg/kg.	Acceptable

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Study No./Type (MRID)	Reported Results	TB Evaluation
(4) 89/SKR004/0341 Bacterial DNA damage (412562-04)	Positive for primary DNA damage (differential toxicity) in repair-deficient E. coli, with/without activation (at 1000 ug/mL and higher).	Acceptable
(5) 102002-M-02289 DNA damage (repair) by UDS (412562-03)	Negative for UDS in HeLa cells exposed up to 10,000 ug/mL, both with/without activation.	Acceptable

B. Interpretation (Roger Ben-Dyke, September 29, 1989)

We agree with both the summary of test results as provided by the registrant's consultant, namely, that sodium chlorate appears to be neither mutagenic nor clastogenic in adequate assays submitted to date, as well as the interpretive caution placed against the singular positive in the bacterial (E. coli) repair test. Since the mammalian repair assay (UDS) was also negative, his overall conclusion that "sodium chlorate does not pose a significant genotoxic hazard" is defensible.

Attachments (DERs)

Reviewed By: Irving Mauer, Ph.D., Geneticist
Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch I - IRS (H7509C)

DATA EVALUATION RECORD 008504

I. SUMMARY

MRID No.: 412[illegible]2-01
ID No.: 91 TX 0022
RD Record No.: S-396696
Caswell No.: 753
Project No.: 1-1718

Study Type: Mutagenicity - Gene Mutation in Bacteria (Ames Test)

Chemical: Sodium chlorate

Sponsor: Kerr McGee Chemical (for the SCTF)

Testing Facility: Life Science Research
Suffolk, UK

Title of Report: Sodium Chlorate: Assessment of Mutagenic Potential in Histidine Auxotrophs of Salmonella typhimurium (The Ames Test)

Authors: K. May

Study Number: LSR Schedule No.: SKR/001
LSR Report No.: 89/SKR001/0285

Date of Issue: August 14, 1989

TB Conclusions:

Negative for inducing reverse gene mutation (his$^-$ to his$^+$) in Ames (bacterial) strains of Salmonella typhimurium exposed with/without activation up to 5000 ug/plate (limit dose).

Classification (Core-Grade): ACCEPTABLE.

II. DETAILED REVIEW

A. Test Material - Sodium chlorate

Description: White crystals
Batch (Lot): (Not stated)
Purity (%): 99.9 (sodium chromate, 1.9 ppm)
Solvent/Carrier/Diluent: Distilled water (DW)

B. Test Organism - Cultures of bacteria

Species: Salmonella typhimurium LT2
Strains: TA 98, TA 1538, TA 100, TA 1535, TA 1537 (his$^-$)
Source: Bruce Ames
UCal (Berkeley)

C. Study Design (Protocol) - This study was designed to assess the mutagenic potential of sodium chlorate when administered in vitro to the Ames battery of S. typhimurium strains, according to established Agency guidelines for this type of assay.

Statements of Quality Assurance measures (inspections/audits) as well as of adherence to Good Laboratory Practice (GLP) were both provided.

D. Procedures/Methods of Analysis - Following preliminary cytotoxicity testing in one of the tester strains (TA98 treated at concentrations up to 5000 ug/plate), all five strains were incubated at 37 °C in pour-plate assays to five concentrations of test article (in triplicate), both in the absence and presence of a mammalian metabolic activation system consisting of the post-mitochondrial fraction (S9) of liver homogenates from young male CD rats pretreated with Aroclor 1254, plus NADP(H)-generating cofactors. In addition to diluent controls (DW), other cultures were treated with their appropriate mutagens*, to serve as positive controls.

*Non-activation: 2-Sodium azide (NaAz, 2 ug/plate)--TA 1535, TA 100.
9-Aminoacridine (AAc, 50 ug/plate)--TA 1537.
2-Nitrofluorene (NF, 5 ug/plate)--TA 1538, TA 98.

Activation: Aminoanthracene (AAnth, 5 ug/plate)--TA 1535.
Benzo(a)pyrene (BP, 5 ug/plate)--TA 1537, TA 1538, TA 100, TA 98.

Two days later, mutant revertent (his$^+$) colonies were counted. Growth of the background lawn of non-revertents on minimal plates was also verified (as a measure of toxicity), and other appropriate procedural controls were summarized in five Appendices of the Final Report. Two separate mutagenicity trials in all strains were conducted.

E. Results:

In the preliminary testing, no cytotoxicity was evident in TA 98 cultures exposed at any concentration of test article. Therefore 5000 ug/plate was selected as the (limit) HDT.

In neither experiment were any increases over DW controls in revertent colonies recorded at any dose (Report Tables 1-5, attached here). In contrast all positive controls responded appropriately, with significant increases 7.5 to 50-plus times background.

The author concluded that sodium chlorate was not mutagenic in these Ames Tests.

F. TB Evaluation: Acceptable

Attachment (Data Report Tables)

ATTACHMENTS

(Data Tables From the Final Report)

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RIN 2906-01

DER/MRID No. 462562-01

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