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DATA EVALUATION RECORD 008504

I. SUMMARY

MRID No.: 412562-02
ID No.: 91 TX 0022
RD Record No.: S-396696
Caswell No.: 753
Project No.: 1-1718

Study Type: Mutagenicity,- Gene Mutation in Mammalian Cells in vitro (V79/HGPRT)

Chemical: Sodium chlorate

Sponsor: Kerr McGee Chemical (for the SCTF)

Testing Facility: Life Science Research
Suffolk, UK

Title of Report: Sodium Chlorate: Investigation of Mutagenic Activity at the HGPRT Locus in a Chinese Hamster V79 Cell Mutation System

Authors: G. Hodson-Walker

Study Number: LSR Schedule No.: SKR/002
LSR Report No.: 89/SKR002/0631

Date of Issue: September 18, 1989

TB Conclusions:

Negative for inducing forward mutation at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus in Chinese hamster lung (V79) cells (HGPRT $^{+}$, $^{-}$), exposed in non-activated (-S9) and activated (+S9) culture to test article up to the limit dose (5000 ug/mL).

Classification (Core-Grade): ACCEPTABLE.

II. DETAILED REVIEW

A. Test Material - Sodium chlorate

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

B. Test Organism - Mammalian cell strain

Species: Chinese hamster (lung), V79
Strains: Clone 9-3/12 ($HGPRT^{+/-}$)
Source: Shell Research
Sittingbourne (UK)

C. Study Design (Protocol) - This study was designed to assess the mutagenic potential of sodium chlorate at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus when administered in vitro to Chinese hamster lung (V79) cells, according to recognized (published) procedures referenced in the Final Report.

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, duplicate cell cultures of V79 cells were each exposed to five (5) concentrations of test article, 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 co-factors (S9-Mix). Following 3 hr treatment, cultures were washed free of treatment medium, re-suspended in fresh medium for a week (for mutant expression), then exposed for 2 to 3 hr to 6-thioguanine (TG) which selects for presumed forward mutant colonies ($HGPRT^{-/-}$), and against all other genotypes at this locus. After a further 6 days selection, TG-resistant (TG^r) colonies (presumed $HGPRT^{-/-}$) were fixed in methanol and prepared for microscopic examination by conventional cytological methods. Coded Giesma-stained slides were scored by eye for mutant colonies, and mutant frequencies (MF) calculated according to the following formula:

$$MF = \frac{\text{No. of Cells Plated for PE}^*}{\text{Mean No. of PE Colonies}} \times \text{Mean No. of 6-TG}^r \text{ Colonies}$$

*PE = Plating efficiency

In addition to solvent (DW) controls, other cultures were treated with the mutagens ethylmethansulfonate (EMS, 1000 ug/mL) or dimethylbenzanthracene (DMBA, 10 ug/mL) to serve as positive controls for, respectively, the non-activated (-S9) and activated (+S9) test series.

The entire assay was repeated once.

E. Results:

In preliminary testing, no evidence of cytotoxicity was found up to the limit dose; hence the HDT selected was 5000 ug/mL, with four lower concentrations to fill out the treatment schedule for the main assays.

Mutation data from both main assays were displayed graphically (Figures 1, 2), as well as in detailed tabulations (Report Tables 3, 4---Trial-I; Report Tables 6, 7---Trial-II), and summarized in Report Tables 8, 9 (attached to this DER).

Although sporadic increases in mutation rates were observed (single cultures, 8 and 40 ug/mL), there was no evidence of consistent dose-related changes in either trial (Report Tables 8, 9). In contrast, both positive controls responded appropriately 30 to 80 times background.

Hence the study author concluded that sodium chlorate was non-mutagenic in V79 cells here.

F. TB Evaluation: Acceptable

Attachment (Data Tables)

RIN 2906-01

DER/MRID No. 413562-02

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