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CASWELL FILE

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DATA EVALUATION RECORD

I. SUMMARY

MRID No.: 404575-22
PC No.: 080805
RD Record No.: S-402936
EPA ID No.: 080805
Tox Chem. No.: 097
Project No.: 1-2487

Study Type: (84-4) Mutagenicity - DNA damage/repair in vitro (HPC/UDS)

Chemical: Prometryn technical

Synonym: G 34 161 techn.

Sponsor: Ciba-Geigy, Greensboro, NC

Testing Facility: Ciba-Geigy, Basel

Title of Report: Autoradiographic DNA Repair Test on Rat Hepatocytes

Authors: I. Bonas, K. Mennle, E. Puri

Study Number: 34161 TECH

Date Issued: May 24, 1984

Conclusions:

Negative for DNA repair in rat hepatocyte cultures.

TB-I Evaluation: Acceptable.

II. DETAILED REVIEW

A. Test Material - G 34 161 techn.

Description: [Not stated]
Batch (Lot): 1045
Purity (%): 100
Solvent/carrier/diluent: Dimethylsulfoxide (DMSO)

B. Test Organism - Primary hepatocyte cultures

Species: Rat
Strain: Tif-RAlf (SPF)
Age:
Weights - males (only): 170-350 g
Source: Ciba-Geigy Tierfarm, Sisseln (Schweiz)

C. Study Design (Protocol) - This study was designed to determine the genotoxic potential of prometryn when administered in vitro to primary rat hepatocyte cultures, according to referenced procedures.

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

D. Procedures/Methods of Analysis - Following preliminary cytotoxicity testing, freshly isolated male rat hepatocytes were cultured on gelatinized coverslips under appropriate culture medium and exposed to a series of four preselected concentrations of test material, concurrent with the addition of 1 uCi/mL tritiated thymidine (^{3}HTdR, of spec. act. = 23.8 Ci/mM). After 5 hr incubation in this cocktail, the coverslip cultures were washed free of treatment media, fixed in Carnoy's and mounted cell-side out onto standard glass microscope slides. These slide cultures were " . . . prepared for autoradiography"*, exposed for 6 days and (finally) stained with H&E. In addition to concurrent negative (solvent) controls, DMN served as positive control.

After determining the background counts "in cell-free areas"*, 50 nuclei per slide (3 slides per test dose group) were scored for nuclear silver grains, net nuclear grain (NNG) counts calculated (absolute count over nuclei less average of three contiguous cytoplasmic counts).

E. Results -

[Net count and count distribution data are provided in Tables 2 and 3, individual test slide data in Tables 5 through 11, and background (historical) data in Tables 3 and 4.]

In cytotoxic testing, cell viability was compromised at doses exceeding 156.25 ug/mL (69% and less viable cells). Hence this level was selected as the HDT, with three lower levels (1.25, 6.25 and 31.25 ug/mL) to fill out the dose schedule for the main assay.

In the main assay no increased NNG was found at any test dose (Table 2, attached here) with only a minority of cells in repair (Table 3, attached). By contrast, DMN-treated cultures provided the expected positive repair response (Tables 2, 3).

F. TB Evaluation - Acceptable

Attachment (Data Tables)

*No further procedural details were provided in the Final Report, but an (included) earlier reporrt recorded these items.

RIN # 0615-00

MRID # 40457522 (DEKS)

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