TDMS | DATA EVALUATION RECORD | PAGE OF

CASE | PM

CHEM Chlorsulfuron (formerly DPX-W4189)

002654

BRANCH Toxicology DISC | TOPIC Mutagenicity

FORMULATION Technical (Information known to reviewer)

FICHE/MASTER ID | CONTENT CAT

The Hepatocyte Primary Culture/DNA Repair Assay on Compound 12,700 Using Rat Hepatocytes in Culture
C. Tong, T. Shimada and G. M. Williams November 15, 1981
Naylor Dana Institute
NDI Experimental Nos: 092381 CT, 092981 CT
NDI Notebook No: CT-44, Pages 33-60
HLO-794-81 MR-0581-920

SUBST. CLASS =

OTHER SUBJECT DESCRIPTORS

DIRECT RVW TIME = 2 hours | START-DATE | END DATE

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Conclusion:

A. This study is scientifically valid.
B. Chlorsulfuron, when assayed twice in the rat hepatocyte primary culture (HPC)/DNA Repair Assay at the highest nontoxic doses (0.2 and 0.04 mg/ml) did not induce DNA Repair.
C. This study generally conforms to EPA Proposed Guidelines in Section 163.84-4 (Federal Register, 43: 37392, 8/22/78).

Methods:

Hepatocyte primary cultures were prepared by perfusion of anesthetized adult male Fisher 344 rats with a collagenase solution. The livers were removed and mechanically dissociated.

Dilutions of 5 X 10^5 hepatocytes were treated simultaneously with 3H-thymidine and chlorsulfuron (purity,94%) in five logarithmically decreasing concentrations on triplicate coverslips. Positive (2-aminofluorene), negative (fluorene) and solvent (DMSO) controls, as well as untreated cell controls, were tested. The first test included chlorsulfuron test concentrations which ranged from 0.0002 to 2.0 mg/ml. The second test used concentrations of 0.0004 to 4.0 mg/ml.

After treatment, coverslips were rinsed in sodium citrate to swell the nuclei. Seven-day autoradiographs were made and cells were stained with hematoxylin and eosin.

Between 5 and 20 cells randomly selected from each coverslip quadrant were counted. Results were quantified by the net increase in nuclear grains induced by the test chemical; background counts were determined for each necleus. Positive results are declared when the minimum net grain count of 5 per nucleus is consistently observed in triplicate coverslips throughout three experiments. Cytoxicity was by morphological criterion and is identified by the absence of S-phase cells in the autoradiograph. Negative results are obtained if the net nuclear count is less than five at the highest non-toxic dose.

Results:

The first test showed cytotoxicity with chlorsulfuron at a concentration of 2.0 mg/ml; the highest non-toxic dose was 0.2 mg/ml. The second test showed cytotoxicity with 0.4 mg/ml; the highest non-toxic dose was 0.04 mg/ml.

The negative control (fluorene at either 5 X 10^{-5} or 1 X 10^{-4}M), the solvent control (DMSO at 10%) and chlorsulfuron at concentrations of 0.2 mg/ml or less, showed net grains per nucleus counts of from 0.2 to 4.2. The positive control (2-aminofluorene at 5 X 10^{-5} or 1 X 10^{-4}M) showed net counts of from 128 to 145.

Discussion:

This study was conducted by acceptable methods and the collected data support the reported conclusions.