US EPA ARCHIVE DOCUMENT

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

AUG 20 1986

005374

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Response to Toxicology Branch Evaluation of Acetochlor DNA Repair Assay in Hepatocytes. EPA ID No. 524-348; TOX PN #1411/1412; Caswell #003B

TO: Robert Taylor (25)
Registration Division (TS-767)

FROM: D. Stephen Saunders, Ph.D. DSS 8/15/86
Toxicologist, Section V
TOX/HED (TS-769)

THRU: Irving Mauer, Ph.D. 08-20-86
Senior Geneticist, Toxicology Branch
and
Laurence D. Chitlik, DABT
Head, Section V, Toxicology Branch Concur for LDC 8-19-86
and
Theodore M. Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division

Action Requested

Review and comment on the response submitted by the Registrant regarding the Toxicology Branch evaluation of the rat hepatocyte DNA repair assay conducted with acetochlor, which was originally classified as Unacceptable data.

Recommendation

It is recommended that the acetochlor rat hepatocyte DNA repair assay (study #PK 82-151 [Monsanto]/PH 311-MO-001-82 [Pharmakon]) be upgraded to Acceptable status. No evidence of mutagenicity was presented in this study, and acetochlor should be considered as negative for DNA damage in this assay.

(con't)

1 of 7

Discussion

Cited Deficiency #1: The purity of the test material was not stated in the study report.

Company response: "The test article, acetochlor (MON 097) was supplied as a pale yellow liquid of 99.7% purity. ...This information was inadvertently omitted from from the final report and has since been added as an addendum (dated Sept. 11, 1985, see attached)."

EPA Comment: This deficiency is corrected by the submitted additional information.

Cited Deficiency #2: The method for calculating doses was not stated. Since the doses were reported as "ug/well", and the test substance was supplied as a liquid, the density and purity of the test material were required to calculate doses. If the investigators assumed a density of 1.0 and purity of 100%, it should be so stated.

Company response: "A weighed aliquot of the test article was dissolved in DMSO and serially diluted. 20 ul of each dilution were added to wells containing cells and media in a final volume of 2 ml. Final concentrations of the test article were expressed as ug/well or ug/ml. The Pharmakon dose preparation sheets have been included as part of the report addendum (attached)."

EPA Comment: This deficiency is corrected by the submitted additional information.

Cited Deficiency #3: The criteria for assessing cytotoxicity were not stated.

Company response: "As indicated in the attached letter from the study director: 'Cytotoxicity is noted by cell detachment, abnormal cell morphology, unusual cell staining and overall decrease in grains relative to the solvent and untreated controls.' Data on these cells in not routinely included in final reports but can be found in the raw data at the testing laboratory."

EPA Comment: This deficiency is corrected by the submitted additional information. The criteria used by the investigators to establish cytotoxicity (detachment, altered morphology, etc.) are fairly standard, and Toxicology Branch is satisfied that potentially positive data have not been discarded due to inappropriate definitions of cytotoxicity.

DSS:TOX/HED:8-15-86:FILE 2RESP3B

2