Reviewed by: Whang ang, Ph.D. 7/26/88
Secondary Reviewers Marcia van Gemert, Ph.D. 7/27/88
Kerry Dearfield, Ph.D. 7.26.88
Section III, Toxicology Branch (TS-769c)

DATA EVALUATION REPORT (DER)

CASWELL FILE

STUDY TYPE: Mutagenicity: CHO/HPRT assay

CHEMICAL: Oxamyl; IND 1410

EPA ACCESSION NO.: 406065-10 CASWELL NO.: 561A

EPA RECORD NO.: 222981/222982 EPA PROJECT NO.: 8-0881

SPONSOR: E. I. du Pont de Nemours & Co., Inc.

TESTING LABORATORY: Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours & Co., Inc.

CITATION: Rickard, L. B. (1982). Mutagenicity evaluation of IND 1410-196 in the CHO/HPRT assay. Haskell Laboratory; Report No.: 265-82. April 21, 1982. Submitted by E. I. du Pont de Nemours & Co., Inc.; April 29, 1988.

SUMMARY: Under the conditions of this study, IND 1410-196 did not induce an increase in the number of HPRT-deficient mutants relative to the controls in the presence or absence of metabolic activation. The study is classified as Unacceptable for the reason presented in the Discussion Section of this DER.

METHODS AND MATERIALS:

Test Compound: IND1410-196; Oxamyl (toxicological sample which is different from the technical) 97.1% purity. White crystalline solid.

Cells: BH4 clone of the Chinese hamster ovary-K1 (CHO-K1) cell line, which was obtained from Dr. A. W. Hsie at Oak Ridge National Laboratory, TN;

Positive indicator: 322 uM methanesulfonic acid, ethyl ester (EMS), Lot # 85C-01431 (Sigma)
7.8 uM 9,10-dimethyl-,1,2-benzanthrancene (DMBA), Lot # 19C-0254 (SIGMA)

Solvent for test agent: dimethylsulfoxide (DMSO) for DMBA
phosphate buffered saline(PBS) for test article and EMS

Abbreviations: CHO = Chinese hamster ovary
HPRT = hypoxanthine-guanine phosphoribosyl transferase

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EXPERIMENTAL PROCEDURES:

The experimental procedures were an adaptation of the HPRT Gene Mutation Assay in Chinese Hamster Ovary Cells. These experimental methods were developed by Dr. A. W. Hsie at Oak Ridge National Laboratory (Muta. Res. 86: 193-214, 1981). The procedures as presented in the submitted report were excerpted and presented in the Appendix; they will not be repeated here. Methods for statistical analysis are also presented in the Appendix.

RESULTS:

Phosphate buffered saline was found to be the solvent for the test chemical; the limit solubility for IND 1410-196 was 200 mg/ml.

The effects of S-9 protein level on cytotoxicity were evaluated. It was found that, at concentrations of 175 and 300 uM IND 1410-196, 1 mg of S-9 protein/ml of medium was the appropriate concentration to be used in the activation assay (Table 1).

Cytotoxicity tests showed that concentration-related cytotoxic effects as indicated by decreased cell survival were observed in both nonactivated (Tables 2 & 3) and activated (Tables 5 & 6) assays. Cell survivals at the top concentrations used were in the acceptable range for adequate tests.

Results of mutagenicity assays with and without metabolic activation did not show any significant increase in the number of mutants in IND 1410-196 treated cultures (Tables 2, 3, 4, 5, 6, and 7).

DISCUSSION AND CONCLUSION:

The chemical, IND 1410-196, was tested for mutagenic activity at concentrations ranging from 25 to 1200 uM in CHO cells. Cytotoxicity tests showed that at concentrations of 750 uM or greater, the test chemical was increasingly cytotoxic in the nonactivated assays. The results of mutagenicity assays with and without metabolic activation indicated that IND 1410-196 did not induce an increase in the number of HPRT-deficient mutants relato the controls. Therefore, the test agent was not mutagenic under these assay conditions.

There is a question concerning the test article, IND 1410-196. The registrant informed the Agency during a meeting held on

July 12, 1988 that IND 1410-196 is synthesized in the laboratory for toxicological testing, and it does not contain three contaminants as does the technical grade. The registrant has been requested by the Agency to provide a logical explanation for this difference. Under the presence circumstances, this study is classified as Unacceptable. After receipt and satisfactory evaluation of the explanation concerning the test article, this study may be upgraded to acceptable.

OXAMYL

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