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

OCT 22 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: Review of supplementary data for the chemical Bis(isopropylamino)-6-methoxy-s-triazine (Prometon Tech) under a Phase 4 Data Call-In

EPA IDENTIFICATION NUMBERS: EPA MRID No's. - 420261-01
420261-02
Caswell No. - 539G
HED Project No. - 2-0306

FROM: SanYvette Williams, D.V.M. 10/15/92
Review Section IV, Tox. Branch II (H7509C)

TO: Thomas Luminello/ Linda DeLuise PM 52
Reregistration Division (CS1)

THRU: Elizabeth Doyle, Ph.D. E.A. Doyle 10/16/92
Section IV, Tox. Branch II (H7509C)

and

Marcia van Gemert, Ph.D., Chief 10/19/92
Toxicology Branch II
Health Effects Division (H7509C)

Registrant: Ciba-Geigy Corporation

Action Requested: Toxicology was requested to review the submitted supplementary data (MRID #423182-03 and 423182-04) to determine whether they satisfy requirements when considered with the original data (MRID #419843-02/406364-02 and MRID # 419843-03/406364-03).

1. Supplemental Information Micronucleus Test, Rat MRID# 423182-03 (Lab Study No.: 871355)

A second supplemental data package (dated May 8, 1992) was submitted in response to a letter from the Agency dated April 24, 1992. Responses to the following information were provided as a basis to upgrade the original micronucleus study:

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a. Utilization of rat versus mouse

This reviewer agrees with the registrants comments which reference the Agency's guidelines which stating that, "while testing in mice is recommended, any appropriate mammalian species may be used."

b. "... selection of the highest dose level is not adequately explained" and "there is no indication whether 648 mg/kg was a clinical MTD or manifested target organ toxicity."

This reviewer concurs with the registrant that evidence of death in one male and female at 648 mg/kg dose group and one female at 324 mg/kg/dose group is evidence of a dose- and treatment-related response indicating that an MTD of 648 mg/kg was achieved or exceeded.

c. "The positive control data is inappropriate."

The registrant claims that the positive control cause significantly increased (2-6 times; $p < 0.05$) micronuclei over concurrent controls, and within this labs historical control values. This reviewer finds this response acceptable.

d. Sampling times

The registrant concurs with the original reviewer that sampling times were appropriate. Therefore, there is no reason for a further re-test.

Conclusion: Since all deficiencies appear to have been satisfied (without re-review of the study itself), this study, in conjunction with MRID # 419843-02, can be classified acceptable.

2. Supplemental Information: DNA repair test MRID #423182-04 (Lab Study No.: 871354

A second supplement data package (dated May 8, 1992) was submitted in response to a letter from the Agency dated April 24, 1992. It referred to the DNA repair test (MRID # 419843-03) in rat hepatocytes, where specific cytotoxicity had not been provided for the highest dose selected.

In response, slides from the original assay were reevaluated and a confirmatory experiment performed. Results of both indicate that at concentrations of 400 ug/ml, evidence of hepatocyte toxicity was evidenced by the increase of pycnotic cells.

Conclusion(s): The deficiency of Prometon for the DNA repair test has been satisfactorily addressed and can now be classified acceptable in conjunction with MRID # 419843-03.