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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

NOV 14 1991

Subject: Prodiamine
ID Number 55947-UR
Tox Chem No. 727A
Project No. 1-2204

From: John H.S. Chen, D.V.M. John H S Chen 11/6/91
Review Section I
Toxicology Branch II
Health Effects Division (H7509C)

To: Joanne I. Miller, PM 23
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Thru: Yiannakis M. Ioannou, Ph.D., Section Head J M Ioannou 11/13/91
Review Section I
Toxicology Branch II
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and

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Toxicology Branch II
Health Effects Division (H7509C)

Sponsor: Sandoz Crop Protection Corporation
Des Plaines, Illinois 60018

Action Requested:

1. Review of the Attached Draft of An EPA Fact Sheet for Prodiamine;

2. What Data Are Needed to Determine the Risks Associated with the Use of This New Chemical (Nonfood use herbicide)?

3. Do the Risks Override Conditional Registration of This New Chemical?

Recommendation:

1. The following errors in toxicology data have been corrected in the attached draft of an EPA fact sheet for prodiamine:

Page 5: Acute Dermal Toxicity Category III instead of IV

Primary Eye Irritation Toxicity Category III instead of IV

Acute Inhalation Toxicity Category III instead of IV

Acute Dermal Toxicity Category (Barricade 65 WDG Herbicide) III instead of IV

Acute Inhalation Toxicity Category (Barricade 65 WDG Herbicide) III instead of IV

Page 6: First Ames assay - add 5000 ug/plate

Third Ames assay - add 0.3-100 ug/plate

Mouse lymphoma mutation assay - add 1, 10, 40, 60, 80, 100 ug/ml in nonactivated study

Page 7: 2-Year Feeding/Carcinogenic Mouse Study - F: 0, 6.8, 64.6, and 646.2 mg/kg/day instead of 0, 2.3, 9.1, 37, and 151 mg/kg/day

2-Year Feeding/Carcinogenic Rat Study - add "receiving 3200 ppm" after "in both males and females"

2. Based on the HED Peer Review Committee's recommendation, additional acute and subchronic neurotoxicity studies with prodiamine in rats and also a subchronic study in rats to investigate thyroid effects are required to determine the risks associated with the use of this new chemical. In addition, the Committee also recommended that the Reference Dose Approach (RFD) should be used for quantitation of human risk (See also Peer Review Document on Prodiamine 6/10/91 G. Burin).

3. Toxicology Branch II believes that the positive results from neurotoxicity studies with prodiamine in rats will definitely have a potential behavioral effect of this new chemical on human risk. Since the subchronic study in rats to investigate the thyroid effect is designed only to assess the role of thyroid gland dysfunction in follicular cell neoplasia, the findings of such a study will not have any effect to alter the thyroid tumor results obtained from the 2-year feeding/carcinogenic study with prodiamine in rats previously submitted.