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

APR 23 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Baygon; Supplimentary Data, Toxicity in Mouse Oncogenicity Study, NOELs Dog and Rat Feeding Studies, Metabolism

TO: Jay Ellenberger, PM-12
Registration Division (TS-767)

FROM: Robert P. Zendzian Ph. D. 3/12/84
Toxicology Branch
HED (TS-769)

THROUGH: William Butler, Head 4/5/84
Review Section III

William Burnam, Chief 4/20/84
Toxicology Branch

Compound, Baygon®

Registration # 2F1244

Accession # 072245

Tox Chem # 508

Background

In 1982 the registrant submitted a 2-year mouse oncogenicity study for review. In my memo of Aug 16, 1982 I submitted a review of the study which questioned the high doses utilized which were 11 (male) and 13 (female) times the acute oral toxicity in rats. Acute data for mice was not available. I specifically requested the following information.

1. An acute oral LD_{50} in males and females of the strain of mice used for the oncogenicity study.

2. A stability test of Baygon in the mouse diet at the doses used in the studies.

3. Photo or xerographic copies of the laboratory records of dose preparation for this study.

4. If the first three requirements do not clarify the toxicity discrepency, a metabolism study utilizing radio labeled Baygon in feed may be necessasry.

My memo also reminded the registrant of Dr Dykstra's requirement for subchronic studies in rat and dog to establish NOELs for cholinesterase inhibition in plasma, RBC and brain.

The registrant also brings up the request for additional metabolism data in order to determine if O-isopropoxyphenol is a metabolite of Baygon in the rat. This matter has been settled and no additional data on the identification of Baygon metabolites in the rat is required.

Registrant's Submission

The registrant has submitted data on the LD_{50} of baygon in the CD-1 mice (Report No 38809). For stability data he has resubmitted the report of the 2-year mouse study (report No 69686). The registrant does not have copies of the laboratory records of diet preparation for this study.

The registrant submits that chronic studies now in progress in the rat and dog will supply the NOEL data requested by Dr Dykstra. The registrant submitted summary tables of data on cholinesterase inhibition from the chronic rat and dog studies.

Discussion

The data submitted by the registrant does not solve the problem associated with the toxicity of baygon in the 2-year mouse study. The report of acute data is incomplete and does not provide information on the material tested and the individual dose-results. Even accepting the mouse data at face value makes the problem worse for the mouse appears to be no less sensitive acutely to baygon and possibly more sensitive ~~acutely~~ than the rat. Thus the difference between acute and chronic lethality of baygon in the mouse becomes greater.

The stability data included with the report consists of the summary pages of the stability analysis and is thus incomplete. In addition the 2-year study used two different materials, technical (99.9%) for the first 6 weeks of the study and a 90% concentration of propoxur [redacted] the remainder of the study. The report does not specify what was tested. It is obvious that both materials should have been tested.

Information which may reveal an inert ingredient is not released

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Conclusion

1) A bioavailabiity study of radio-labeled baygon in feed is required in order to determine the mechanism of the 11 to 13 fold decrease in lethality in the feeding study.

2) The chronic rat and dog studies can be used in place of the 90-day studies to determine no effect levels for cholinesterase inhibition. Upon completion of the studies and submission of their final reports an evaluation as to NOELs will be made. This evaluation cannot be made on incomplete or preliminary data. Thus the data submitted at this time cannot be used to determine a NOEL.