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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Mr. John S. Thornton
Mobay Corporation
Agricultural Chemicals Division
P.O. Box 4913, Hawthorn Road
Kansas City, MO 64120-0013

Dear Mr. Thornton:

Subject: Metribuzin Technical (Response to Registration Standard)
EPA Registration No. 3125-270
Sencor 50% Wettable Powder for Repackaging
EPA Registration No. 3125-305
Sencor 50% Wettable Powder
EPA Registration No. 3125-277
Sencor 70% Wettable Powder
EPA Registration No. 3125-294
Sencor 4 Flowable
EPA Registration No. 3125-314
Sencor DF 75% Dry Flowable
EPA Registration No. 3125-325
Your Letters Dated May 3, October 31, December 3 and 30, 1985, and February 17, March 31, and June 9, 1986

The scientific review and evaluation of the data submitted above in support of the Metribuzin Registration Standard have been completed. The following are our conclusions/comments.

I. PRODUCT CHEMISTRY

A. Description of Beginning Materials and Manufacturing Process (Guidelines Reference No. [GRN] 61-2)

- A more detailed description of the manufacturing process for the technical material is still required, i.e., description of each step of the process, any pressure and temperature conditions required for maximum yield, quality control measures for the technical and manufacturing-use products, etc. A data gap still exists here.

B. Discussion of the Formation of Impurities (GRN 61-3)

- The information submitted on impurities satisfies this requirement.

C. Preliminary Analysis (GRN 62-1)

- Analysis of five more recent production batches is needed (those submitted were from 1978). The batches should be spaced over a time period longer than 1 month. A data gap still exists. We note additional information was submitted on June 12, 1986.

D. Certification of Limits (GRN 62-2)

1. Technical Product--The information submitted appears to be acceptable. However, this information must be submitted on EPA Form 8570-4 (Rev. 2-85). On receipt of the correctly completed form, this data gap will be satisfied.

2. 50% Wettable Powder for Repackaging--The information submitted is acceptable. The data gap for this product is satisfied.

E. Analytical Methods to Verify Certified Limits (GRN 62-3)

- No validation data were submitted for any of these methods. Therefore, a data gap still exists. We note this information was submitted on June 27, 1986.

F. Physical and Chemical Characteristics (GRN 63-2 to 63-20)

- These data gaps are satisfied.

II. RESIDUE CHEMISTRY

Sugarcane Processing Study

A. The available processing study indicates a concentration of 20X for molasses, 5X for bagasse, and none for refined sugar. Since the tolerance on sugarcane is 0.1 ppm, appropriate food additive tolerances would be 2.0 ppm for molasses and 0.5 ppm for bagasse.

B. The deficiency concerning sugarcane processing which was identified on the Registration Standard is resolved.

III. TOXICOLOGY

A. Nine-Week Feeding Study in Rats

1. This study is classified as Core-Supplementary data since only males were examined and the histopathology was limited in scope; these data are ancillary and, as such, do not meet any regulatory requirement.

2. The treatment of male rats with DIC 1468 revealed systemic effects in all four dose groups; however, other than the body systemic effect, the no-observed-effect level for this study is below 3.5 ppm, the lowest dose tested.

3. The main thrust of this study was to establish the dose-time-effect relationship for DIC 1468 in the thyroid. From the data presented, the investigators assumed ". . . that peripheral deiodination of thyroxine triiodothyronine is impaired after administration of up to 900 ppm DIC 1468, so that a secondary increase in thyroid functioning takes place." However, this assumption is difficult to follow from the evidence presented.

4. The conclusion is that treatment with DIC 1468 appears to have an effect on thyroid function but the mechanism and biological significance remain uncertain.

B. Dermal Absorption Protocol

1. The requirement for a dermal absorption study for metribuzin is voided.

2. A copy of the protocol that the Agency is developing is enclosed for your information.

C. Clarification for Mutagenicity Requirements

1. To fulfill the minimum requirements for mutagenicity testing, a primary DNA damage/repair assay and an *in vitro* mammalian point mutation study must be submitted. Studies submitted are discussed below.

2. Studies submitted fulfill the requirement for microbial point mutation tests and *in vivo* cytogenetics tests in mammals with either heritable translocation or dominant lethal studies.

D. Review of Mutagenicity Tests

1. DNA Damage/Repair: Unscheduled DNA Synthesis (UDS) in Primary Rat Hepatocytes (GRN 84-2)

   a. Under the conditions of this test, metribuzin did not cause a significant increase in UDS as measured in this study, whereas the positive control did increase UDS.

   b. This study is acceptable.

2. Gene Mutation in Mammalian Cells In Vitro: CHO/HGPRT Assay (GRN 84-2)

   a. Under the conditions of the study, metribuzin is negative in the CHO/HGPRT mutation assay.

   b. This study is acceptable.

3. These studies satisfy GRN 84-2

E. Acute Inhalation Studies

1. Acute Inhalation Study (Metribuzin)

   a. The LC_{50} is greater than the gravimetric concentration of 648 mg/m^3 (0.648 mg/L) for male and female rats.

   b. This dose is considered the maximum obtainable concentration for the equipment used and produces no compound-related mortality.

   c. This study is classified as Core-Minimum data.

   d. The Toxicity Category is II.

2. Acute Inhalation Toxicity (Sencor 50% Wettable Powder)

   a. The LC_{50} is greater than the gravimetric concentration of 2123 mg/m^3 (2.21 mg/L) for male and female rats.

   b. This dose is considered the maximum obtainable concentration for the equipment used and it produces no compound-related mortality.

   c. This study is classified as Core-Minimum data.

   d. The Toxicity Category is III.

3. These studies satisfy the acute inhalation study (GRN 81-3) requested in Generic Data Requirements Table A and the acute inhalation study (GRN 81-3) requested in Generic Data Requirements Table B.

IV. FISH AND WILDLIFE

Avian Acute Dietary LC_{50} Study

A. Based on the subacute dietary LC_{50} greater than 5000 ppm, the pesticide is considered practically nontoxic to bobwhite quail (upland game bird).

B. This study is scientifically sound and satisfies the Guidelines requirement for the Avian Acute Dietary LC_{50} study.

Sincerely yours,

Robert J. Taylor VTaw
Product Manager (25)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

Enclosure