4-29-92

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

APR 29 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Review of Protocol for Fenoxaprop-ethyl (Tiller® Herbicide) Mouse Onco Study

Shaughnessy No. 128701 Submission No. S372042

TO: Joanne Miller PM 23
RD (H7505C)

FROM: K. E. Whitby, Ph.D.
Section, II
Toxicology Branch II/(HED) (H7509C)

THRU: K. Clark Swentzel 4/28/92
Section Head
Toxicology Branch II/(HED) (H7509C)

and

Marcia van Gemert, Ph.D. 4/28/92
Chief, Toxicology Branch II/(HED) (H7509C)

Requested Action

Review draft protocol and dose selection for mouse onco study which was required by conditional registration of this product.

TBII Response

Protocol Review

1. Page 2, paragraph 7 of the draft protocol states that the study will be performed according to "Combined Toxicity/Oncogenicity Studies" series 83-5 of the Pesticide Assessment Guidelines Subdivision F. The guidelines set forth in §83-5 are intended for studies designed to meet both chronic and oncogenicity requirements. However, in as much as the stated objective of this investigation is to assess the potential oncogenicity of fenoxaprop-ethyl, the study should

be performed in accordance with §83-2. Otherwise the stated objective should be modified accordingly.

2. Page 121 of the Pesticide Assessment Guidelines, Subdivision F §83-2 indicates under (8) Clinical Pathology that "at 12 months 18 months and at sacrifice, a blood smear should be obtained from 10 animals/sex/dosage group. A differential blood count should be performed on blood smears from those animals in the highest dosage group and the controls."

3. Page 11 of the draft protocol under hematology: platelet count and leucocyte differential count have been omitted.

4. Page 11 of the draft protocol under clinical chemistry: electrolytes (i.e. Ca, Cl, Mg, P, K, Na), albumin, blood creatinine, total serum protein, and creatinine phosphokinase (CPK) were omitted. (These are required for §83-5.)

5. Page 13 of the draft protocol under necropsy: the list of samples to be collected from all animals excluded epididymides.

6. Page 13 of the draft protocol under necropsy: thyroid/parathyroid were omitted from organ weights.

7. Page 14 of the draft protocol under statistical analysis: body weight gain and food consumption were omitted.

Dose Selection Review

The Registrant has indicated, mutual concurrence is essential prior to initiation of this study. However, based on the available data base TBII is not of the opinion that there adequate preliminary studies/evidence in the mouse to support selection of doses for a mouse onco study. Our recommendation would be to perform a 90 day subacute (range-finding) study with doses high enough to detect significant changes in body weight gain and histopathology in animals surviving to completion of the study.