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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Fenoxaprop-ethyl: Summary of 90-day study in mice to support dose selection for a carcinogenicity study

TO: Joanne Miller/Eugene Wilson PM 23
Registration Division

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CASE	192866
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SUBMISSION:	S440581
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CASWELL NO.	431C
REGISTRANT:	Hoechst Celanese

Requested Action

Review 90-day study summary to determine if dose selection for a carcinogenicity study in mice is appropriate.

Submission

The registrant performed a 90-day study in mice, at the suggestion of TB II, in order to determine the maximum tolerated dose (MTD). This submission contains a summary of the data on which the selection of dosages for the carcinogenicity study was based.

The test material was mixed with the diet at levels of 0, 320, 640 or 1280 ppm. The summary indicates that there was no mortality during the study. Also, body weights and food consumption were not affected at any level. The following effects were reported at 320

ppm and above: "clinical signs of intoxication (swollen abdomen, flanks drawn in, straddling hind limbs and bristling coat); slight effects on hematology/clinical chemistry (anemia as shown by reticulocytosis, and increased MCV); liver function (increased alkaline phosphatase and albumin and decreased bilirubin); organ weight changes (liver [M, +80%; F, +50%]), kidneys and adrenals (M only); histopathology (centrilobular hepatocellular hypertrophy, increased incidence of single cell necrosis (M, 16/20; F, 6/20; grade 2); peroxisome proliferation, vacuolation of tubular cells (females only at 320 ppm), increased extramedullary erythropoiesis (males) and increased marker enzymes (catalase, malic enzyme, LDH, GPDH)." An examination of the histopathology data revealed that most of the single cell necrosis was graded 1 in severity at this dietary level but increased at the higher levels. Additional effects as well as increased severity of the effects noted at 320 ppm were reported at 640 and 1280 ppm.

Based on these results, the registrant recommended 0, 40, 115 and 320 ppm dietary levels for the carcinogenicity study.

Response

It is TB II's opinion that the data in the 90-day mouse study support the registrant's dose selection for the carcinogenicity study in mice.

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