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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Data Gaps for Fenoxaprop-Ethyl

TO: Eugene Wilson PM 23
RD (H7505C)

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

THRU: K. Clark Swentzel 5/28/91
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and

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Caswell No. 431C
Shaughnessy No. 128701
HED Project No. 1-1173
Registrant: Hoechst Celanese Corporation
Chemical: 2-[4-[(6-chloro-2-benzoxazoly)oxy]phenoxy]propanoic acid, ethyl ester (+-)-
Synonyms: Fenoxaprop-Ethyl
Trade Names: Whip, Acclaim

The purpose of this memorandum is to clarify issues raised in a memorandum dated March 19, 1991 [Whitby (H7509C) to Wilson (H7505C)] regarding data gaps for the subject chemical.

It was recently brought to the attention of Tox Branch II that the Hoechst Celanese Corporation submitted in May of 1986 a response to HED reviews of the teratology studies (Accession number 263034). This submission contained supplements to the following studies:

1) Supplement to Report No. 83.0516 Testing for Embryotoxicity of HOE 033171 in Himalayan Rabbits Following Oral Administration (Initial Report dated September 29, 1983; Study No. G2K0400)

2) Addendum to Project 028776 Embryotoxicity Study in the Rabbit (Dermal Application)

3) Addendum to Project 028765 Embryotoxicity Study in the Rat (Dermal Application)

4) Supplement to Report No. 667/82 An Oral Embryotoxicity Study of HOE 33171 in Himalayan Rabbits [Initial report (A24756) dated October 21, 1982]

5) Supplement to Report No. 613/82 An Oral Embryotoxicity Study of HOE 033171 in Wistar Rats (report dated October 4, 1982) **This study was core grade minimum.**

In keeping with the purpose of this memorandum, the discussion will only comment on item no. four of this submission.

I. Rabbit Teratology Study of HOE 33171 (study no A24756 - oral teratogenicity study in rabbits)

The initial report (Accession No 256667; Study No. A24756) was presented as mean values for food consumption, bodyweights, and organ weights of dams. Autopsy findings in dams, uterine findings, fetal survival rate during a 24 hr post natal incubation period, autopsy, fetal cross section and skeletal data were presented. The results of the clinical examinations were initially reported only in the form of text.

The supplemental information which has been submitted provides the individual clinical data, food consumption, bodyweights, organ weights, and the morphological findings in the fetuses. The clinical and macroscopic findings in the dams and the morphological findings in the fetuses are also provided in a summary table. Fetal morphological findings are listed separately as malformations, anomalies, variations or retardations. Furthermore, statistical analyses were performed on the morphological findings for fetuses and litters separately by the Fisher Exact test (set to detect significance $\leq$ 0.05). The supplemental report also contained a correction for a typographical error, which does not impact upon any conclusions.

The supplemental report indicated that the number of fetuses with an anlage of a short or normally sized 13th rib, uni- or bilateral, was significantly increased at the 200 mg/kg group. Based upon the presentation of the data (continued enclosure 19 p 93 of this submission) it would appear that this finding was significant on both the fetal and litter basis. No other findings in the treated groups indicated a statistically significant increase relative to the control. The supplemental report indicates that the diaphragmatic hernia finding was substance related, as the incidence noted in this study was higher than the historical

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control (only one fetus in their 32 control groups up to that time was observed with this finding).

With regard to food consumption, the initial submission states rabbits were fed with Altromin® K2013 pellets (manufactured by Altromin GmbH, Lage/Lippe) and tap water ad libitum. The report further indicates that each animal also received 40-50 g of autoclaved hay per day. It is not clear whether the hay was made available for feeding or bedding, or whether the values provided represent amount of pelleted chow consumed or hay and chow combined. During the study food consumption was reportedly checked "continually" (frequency interval not specified). The original submission and therefore the DER, consist of tables in which the initial interval for food consumption was days 0-7 (the day of mating was taken as day 0 of pregnancy). The supplemental report provides individual animal data for the initial interval as days 1-7. The means and standard deviations for this interval do not match the previous submission and DER.

Revisions to the Data Evaluation Report

1. The original DER states that a decrease in defecation was reported for 4/15, 3/15, 8/15, and 15/15 females from the 0, 12.5, 50, and 200 mg/kg/day groups. The incidence should be revised to 4/15, 5/15, 10/15, and 15/15.

The results of the analytical tests on concentration and stability have been submitted (MRID 418497-00) for the oral rabbit teratology study (Study No. A24756, Accession No. 256667; start date of study 5/3/82). Dosing solutions were prepared daily at concentrations of 25, 100, 400 g/L. Doses were administered in 0.5 mL sesame seed oil/kg bodyweight. The submitted data (dated February 10, and June 1, 1982) indicate that fenoxaprop-ethyl was stable for three days in sesame seed oil (conditions of storage unspecified). The data (June 1, 1982) further show that the concentration of the active ingredient in the 400 g/L dosing solution ranged between 120-151% of the theoretical concentration 1-72 hours after preparation.

NOTE: Page 3 of the memorandum dated March 19, 1991 [Whitby (H7509C) to Wilson (H7505C)] regarding data gaps for the subject chemical contains an error - under the heading of acute inhalation toxicity of the 97% technical, the memo indicates that the current core grade for this study is invalid. The correct current core grade for this study is core minimum.

CONCLUSION

The Rabbit Teratology Study of HOE 33171 (study no A24756 - oral teratogenicity study in rabbits) should be upgraded to Core-minimum.

1. TOXICOLOGY DATA AVAILABLE

A. Acute Testing

Acute Oral LD_{50} -		
Technical - 97% (rat)	Tox Cat 3 LD_{50} ♂ = 2357 ♀ = 2500 mg/kg	guideline
Technical - 97% (mouse)	Tox Cat 3 LD_{50} ♂ = 4670 ♀ = 5490 mg/kg	minimum
EC - 12.5% (rat)	Tox Cat 3 LD_{50} ♂ = 3310 ♀ = 3400 mg/kg	minimum
0.75 EC - 9.8% a.i. (rat)	Tox Cat 3 LD_{50} ♂ = 2810 ♀ = 2260 mg/kg	minimum
HOE 046360 7.4% pure (rat)	Tox Cat 3 LD_{50} ♂ = 5000 ♀ = 4410 mg/kg	minimum
Tiller Herbicide (EUP) (rat)	Tox Cat 3 LD_{50} ♂ = 4 - 5 ♀ = 1.25 - 2.0 g/kg estimated LD_{50} is 3.06 g/kg	guideline
Acute Intraperitoneal Toxicity -		
Technical - 97% (rat)	LD_{50} ♂ = 739 mg/kg ♀ = 864 mg/kg	
Acute Dermal Toxicity -		
Technical - 97% (♀ rat)	Tox Cat 3 LD_{50} > 2000 mg/kg	minimum
Technical - 97% (rabbit)	Tox Cat 2 LD_{50} > 1000 mg/kg	minimum
EC - 12.5% (rat)	Tox Cat 3 LD_{50} > 2000 mg/kg	minimum
0.75 EC - 9.8% a.i. (rat)	Tox Cat 3 LD_{50} > 2000 mg/kg	minimum
HOE 046360 7.4% pure (rat)	Tox Cat 3 LD_{50} > 5000 mg/kg	minimum
Tiller Herbicide (EUP) (rat)	Tox Cat 3 estim. LD_{50} 4.0 g/kg	guideline
Acute Inhalation Toxicity -		
Technical - 97% (rat)	Physical nature of material prohibited use of higher dosage.	minimum

NOTE: EC = emulsifiable concentrate
HOE = trade name