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

JUN 2 - 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Acute Oral Toxicity Study on DPX-T6376-Intermediate, an impurity in Metsulfuron Methyl

TO: Vickie Walters
PM Team Reviewer (25)
Registration Division (H7505C)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 5/27/93
Toxicology Branch II, Section II,
Health Effects Division (H7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 5/27/93
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D. Marcia van Gemert 5/28/93
Chief, Toxicology Branch II/HFAS/HED (H7509C)

Registrant: E.I. duPont de Nemours & Co., Inc.
Chemical: [redacted]

Synonym: DPX-F6594-3
Submission: S433364
DP Barcode: D186623
Caswell No.: 419H
Case No.: 284309
Identifying No.: 122010
MRID No.: 425459-01
Action Requested: None specified.

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Comment: The Registrant has submitted an acute oral toxicity study on an impurity [IN F6594-3] of Metsulfuron methyl. A previous study was classified Core Supplementary (memo dated 4/26/90). This study has been reviewed, and the DER is attached.

Under the conditions of the study, the acute oral lethal dose (LD_{50}) of IN F6594-3 was greater than 3000 mg/kg, the highest dose tested (due to the limited amount of test material available). The Toxicity Category is III.

(1)

Primary Reviewer: Linda L. Taylor, Ph.D. Linda Lee Taylor 5/27/93
Review Section II, Toxicology Branch II/HED (H7509C)
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DATA EVALUATION REPORT

STUDY TYPE: Acute Oral - Rats (§81-1)

CASWELL NUMBER: 419H

MRID NUMBER: 425459-01

TEST MATERIAL: IN F6594-3 MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

SYNONYMS: [redacted]
DPX-F6594-3

STUDY NUMBER: 4581-876; HLR # 148-91

SPONSOR: DuPont

TESTING FACILITY: Haskell Laboratory for Toxicology and Industrial Medicine; Delaware

TITLE OF REPORT: Acute Oral Toxicity Study with IN F6594-3 in Male and Female Rats

AUTHOR(S): JW Sarver

REPORT ISSUED: August 19, 1991

CONCLUSION: Under the conditions of the study, the acute oral lethal dose (LD_{50}) of IN F6594-3 was greater than 3000 mg/kg, the highest dose tested due to the limited amount of test material available.

TOXICITY CATEGORY: III

CLASSIFICATION: Core-Minimum. This study satisfies the guideline requirements (§81-1) for an acute oral toxicity study in rats.

A. MATERIALS

1. Test compound: IN F6594-3; Description: white solid; Batch #: Medical Research # 4581-876, Haskell # 17,726; Purity: 94.9%; Source: JC Summers (DuPont).

2. Test animals: Species: rat; Strain: Crl:CD®BR; Age: ≈ 7 weeks old; Weight: ♂:206-244 g, ♀:162-184 g; Source: Charles River Breeding Laboratories, Raleigh, NC.

B. STUDY DESIGN

1. Methodology: Groups of ten male and ten female rats were administered the test material (suspensions in Mazola® corn oil) by gavage at dose levels of 1000, 2000, and 3000 mg/kg in a dosage volume that varied with dose (see Table 1, below). The animals were fasted for ≈ 24 hours prior to dosing. No details were provided as to how the animals were selected for this study (randomization). During acclimation (≈ 1 week) and the 14/15-day observation period following dosing, the animals were housed individually and provided with Purina Certified Rodent Chow® # 5002 and water ad libitum. The survivors were weighed and observed for clinical signs of toxicity and mortality during the observation period. All rats found dead or sacrificed at study termination were subjected to a gross pathological examination.

Table 1. Dosing Data

Dose (mg/kg)	ave. fasted body weight (g)	suspension conc. (mg/mL)	ave. dose volume (mL)
MALES			
1000	227	150	1.5
2000	229	200	2.3
3000	232	200	3.5
FEMALES			
1000	172	150	1.1
2000	172	200	1.7
3000	175	200	2.6

2. Dose preparation: The test material was prepared (on the day of dosing) as a suspension in Mazola® corn oil. No attempt was made to measure the stability, homogeneity, or concentration of the test material, and the IN F6594-3 was assumed to be stable under the conditions of the study. Due to synthesis difficulties, insufficient IN F6594-3 was available to test additional doses or to determine an LD_{50}.

C. RESULTS

Deaths occurred up to day 6 after dosing. Due to the limited amount of test material available, an LD_{50} was not determined. The number of deaths at the highest dose tested (3000 mg/kg) suggests that the LD_{50} is greater than 3000 mg/kg [see Table 2, below]. Clinical signs included lethargy, hunched posture, high carriage, discharges (ocular, nasal or oral), and wet/yellow-stained perineums. Body-weight changes ranged from sporadic slight to severe weight loss.

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Table 2. Mortality

Dose (mg/kg)/group	# deaths/# dosed
MALES	
1000	2/10
2000	2/10
3000	1/10
FEMALES	
1000	0/10
2000	1/10
3000	4/10

D. CONCLUSIONS

Under the conditions of the study, the acute oral lethal dose (LD_{50}) of IN F6594-3 was greater than 3000 mg/kg, the highest dose tested due to the limited amount of test material available. This study is classified Core Minimum, and it satisfies the guideline requirement (§81-1) for an acute oral toxicity study in rats. The Toxicity Category for IN F6594-3 is III.

STUDY DEFICIENCIES

Although no analysis of the test material was performed, the doses were prepared just prior to dosing. The information provided on animal selection for inclusion in the study was limited, and the LD_{50} could not be calculated due to the limited amount of test material available. However, the data provide sufficient information for a determination of the Toxicity Category for this impurity of DPX-T6376. TB II concludes that these deficiencies do not compromise the study.