EPA Reviewer and WAM: Marion Copley, D.V.M., D.A.B.T. Marion Copley, Date Nov 23/1998
Registration Action Branch 1 (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D245135
P.C. CODE: 067710

SUBMISSION CODE: S539237
TOX. CHEM. NO.: none

TEST MATERIAL (PURITY): IN-JT333-20 (98.7% JT333, a.i.)

SYNONYMS: Indeno[1,2-*e*][1,3,4]oxadiazine-4a(3*H*)-carboxylic acid, 7-chloro-2,5-dihydro-2-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]-, methyl ester

CITATION: Sarver, J. (1996) Acute oral toxicity study with IN-JT333-20 in male and female rats. E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Elkton Road, P.O. Box 50, Newark, DE 19714. Laboratory Report ID 927-96, November 20, 1996. MRID 44477117. Unpublished.

SPONSOR: DuPont Agricultural Products, E.I. du Pont de Nemours and Company, Barley Mill Plaza, Wilmington, DE 19898

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44477117) five male and five female fasted young adult Crl:CD®BR rats per group were given 10, 30, 50, 100, or 200 mg/kg of IN-JT333-20 (98.7% JT333; Batch no. IN-JT333-20) (in corn oil) by gavage and observed for 14 days.

Two males in the 50 mg/kg group were found dead on days 7 and 11. All males in the 100 mg/kg group were found dead on days 2 through 6, and the males in the 200 mg/kg group were found dead on days 3 through 5. The females in the 50 mg/kg group were found dead on days 6 through 11. All females in the 100 mg/kg group were found dead on days 4 through 12, and the females in the 200 mg/kg group were found dead on days 2 through 5.

Before death, the most often observed clinical signs of toxicity in the decedents included ataxia, piloerection, hunched posture, splayed rear legs, general spasms, tremors, and ruffled fur. The surviving males in the 50 mg/kg group exhibited hunched posture, piloerection, ruffled fur, diarrhea, and/or high carriage. The other surviving rats exhibited piloerection, hunched posture, ruffled fur, stained perineum, and/or diarrhea.

Males in the two low doses gained weight throughout the study. The surviving males in the 50 mg/kg group lost weight during the first week and the surviving females had sporadic weight loss throughout the study. All had an overall weight gain by the end of the study.

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The oral LD_{50} for **males = 52 mg/kg,**
females = 39 mg/kg, and
combined = 47 mg/kg.

IN-JT333-20 is in TOXICITY CATEGORY I based on the LD_{50}.

This acute oral study is classified as acceptable (guideline). This study does satisfy the guideline requirement for an acute oral study (81-1) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: IN-JT333-20

   Description: beige solid
   Lot/Batch #: IN-JT333-20 (Batch number)
   Purity: 98.7%, a.i.
   CAS #: 144171-39-1

2. Vehicle and/or positive control

   Vehicle - corn oil, positive control - none

3. Test animals

   Species: rat
   Strain: Crl:CD®BR
   Age and/or weight at dosing: males: 53-57 days, 204-238 g, females: 60-71 days, 184-225 g
   Source: Charles River Breeding Laboratories, Raleigh, NC
   Acclimation period: ~1 week
   Diet: Purina® Certified Rodent Chow® No. 5002, *ad libitum*
   Water: *ad libitum*
   Housing: individually in suspended, stainless steel, wire-mesh cages
   Environmental conditions:
   Temperature: 23±1 °C
   Humidity: 50±10%
   Air changes: not reported
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 3, 1996; end : August 15, 1996

2. Animal assignment and treatment

Following an overnight fast, five rats/sex/group were given 10, 30, 50, 100, or 200 mg/kg of the test material suspended in corn oil by gavage. The animals were observed for mortality daily. The animals were weighed and observed daily for clinical signs of toxicity with the exception of males and females in the 30 mg/kg group that were not weighed or observed on days 10 and 11. All rats were sacrificed and necropsied at death or at the end of the 14-day observation period.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
10	0/5	0/5	0/10
30	0/5	0/5	0/10
50	2/5	5/5	7/10
100	5/5	5/5	10/10
200	5/5	5/5	10/10

Data taken from p. 14, MRID 44477117.

3. Statistics

Calculation of the female oral LD_{50} was by the method of Finney (Probit Analysis).

II. RESULTS AND DISCUSSION

A. Mortality is in Table 1.

Two males in the 50 mg/kg group were found dead on days 7 and 11. The males in the 100 mg/kg group were found dead on days 2 through 6, and the males in the 200 mg/kg group were found dead on days 3 through 5. The females in the 50 mg/kg group were found dead on days 6 through 11. The females in the 100 mg/kg group were found dead on days 4 through 12, and the females in the 200 mg/kg group were found dead on days 2 through 5.

The oral LD_{50} for males = 52 mg/kg,
females = 39 mg/kg,
combined = 47 mg/kg.

This places IN-JT333-20 in TOXICITY CATEGORY I.

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B. CLINICAL OBSERVATIONS

The most often observed clinical signs of toxicity in the decedents included ataxia, piloerection, hunched posture, splayed rear legs, general spasms, tremors, and ruffled fur. The surviving males in the 50 mg/kg group exhibited hunched posture, piloerection, ruffled fur, diarrhea, and/or high carriage. The other surviving rats exhibited piloerection, hunched posture, ruffled fur, stained perineum, and/or diarrhea.

C. BODY WEIGHT

The males in the two low dose groups gained weight during the study. The surviving males in the 50 mg/kg group lost weight during the first week and the surviving females had sporadic weight loss throughout the study. All had an overall weight gain by the end of the study.

D. NECROPSY

The gross observations were nonspecific.

E. DEFICIENCIES

The air change frequency of the animal room was not reported. This would not affect the study results.