DATA EVALUATION RECORD

7/19/2000

MESOTRIONE (ZA1296 (480 g/L SC Formulation))

Study Type: §81-1, Acute Oral Toxicity

Work Assignment No. 2-01-52D (MRID 44373513)

Prepared for
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Disclaimer

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DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS Number: 870.1100 OPP Guideline Number: §81-1

DP BARCODE: D259369 SUBMISSION CODE: S541375
P.C. CODE: 122990 TOX. CHEM. NO.: None

TEST MATERIAL (PURITY): 480 g/L SC Formulation of ZA1296 [40.5% (w:w) ai]

SYNONYMS: None specified

CITATION: Lees, D., and H. Connolly (1997) ZA1296: acute oral toxicity to the rat of a 480 g/L SC formulation. Zeneca Central Toxicology Laboratory, Macclesfield, Cheshire, UK. Laboratory Report No. CTL/P/4809, Study No. AR6121. August 8, 1997. MRID 44373513. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, DE.

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44373513), five young adult Alpk:AP$_f$SD (Wistar-derived) rats/sex were given a single oral dose of a 480 g/L SC Formulation of ZA1296 [40.5% (w:w) ai] at 5,000 mg/kg. The test substance was administered in deionized water, and the animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

The 480 g/L SC Formulation of ZA1296 is classified as **TOXICITY CATEGORY IV** based on the observed LD_{50} values for both sexes.

All animals survived the 14-day study. No treatment-related signs of toxicity, effects on body weight, or gross pathological abnormalities were observed in male animals. In contrast, diarrhea was observed in all female rats between 1 and 2 days, and slight decreases (5-7% ↓) in weight were observed in 3/5 females between 2 and 7 days. Overall, all females exhibited weight gains, ranging from 13 to 22%. Necropsy revealed enlarged and/or red ovaries in 3/5 females.

This study is classified **acceptable (§81-1)** and satisfies the guideline requirement for an acute oral study 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: 480 g/L SC Formulation of ZA1296
   Description: Tannish brown liquid
   Lot/Batch #: WF2381; 14541-25-03
   Purity: 40.5% ZA1296 (w:w)
   CAS #: Not provided

2. Vehicle: Deionized water

3. Test animals: Species: Rat
   Strain: Alpk:AP$_f$SD (Wistar-derived)
   Age: Young adult
   Weight: 282-300 g males; 212-246 g females
   Source: Barriered Animal Breeding Unit, Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK
   Acclimation period: ≥6 Days
   Diet: (PCD) Special Diet Services Limited, Witham, Essex, UK, ad libitum
   Water: Tap water, ad libitum
   Housing: Five animals per cage, separated by sex, in suspended stainless steel cages
   Environmental conditions:
   Temperature: 21±2 °C
   Humidity: 55±15%
   Air changes: Approximately 25-30 changes/hour
   Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: September - October 1995

2. Animal assignment and treatment: Following an overnight fasting period, ten rats (5 males, 5 females) were given a single oral dose of a 480 g/L SC Formulation of ZA1296 at 5,000 mg/kg by gavage. The test material was administered in deionized water at a standard volume of 10 mL/kg. The animals were observed for signs of systemic toxicity

within 2 hours of dosing, between 4 and 7 hours postdosing, and once daily thereafter for the remainder of the 14 day study. Body weights were recorded on days -1, 0 (immediately prior to dosing), 2, 5, 7, and 14. At 14 days, all animals were sacrificed, necropsied, and examined for gross pathological changes.

3. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: No mortalities occurred during the study.

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

B. Clinical observations: No treatment-related clinical signs were observed in males throughout the study. Diarrhea was observed in all female rats between 1 and 2 days; this effect subsided from all animals by day 3.

C. Body Weight: No treatment-related effect on body weight was observed in male animals, who exhibited an overall (0-14 days) mean (n=4) increase of 33%.[1] Slight decreases (5-7% ↓) in weight were observed in 3/5 females between 2 and 7 days; however, all females exhibited overall increases, ranging from 13 to 22% (mean of 18%).

D. Necropsy: Necropsy after 14 days revealed enlarged and/or red ovaries in 3/5 females. No gross abnormalities were observed in any of the male rats upon necropsy.

E. Deficiencies: There were no deficiencies that affected the validity of the study results.

[1]The body weight of one male was not recorded prior to sacrifice.