DATA EVALUATION RECORD

MESOTRIONE (ZA1296) 7/19/2000

Study Type: §81-6, Dermal Sensitization Study

Work Assignment No. 2-01-52M (MRID 44373522)

Prepared for
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U.S. Environmental Protection Agency
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Disclaimer

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DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS Number: 870.2600 OPP Guideline Number: §81-6

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

TEST MATERIAL (PURITY): ZA1296 (95.1% purity)

SYNONYMS: None specified

CITATION: Robinson, P. (1994) ZA1296: skin sensitisation to the guinea pig. Zeneca Central Toxicology Laboratory, Macclesfield, Cheshire, UK. Laboratory Report No. CTL/P/4506, Study No. GG6226. November 2, 1994. MRID 44373522. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, DE.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44373522) conducted with ZA1296 (95.1% purity) 40 Hsd/Pos:DH albino female guinea pigs (20 test and 20 control) were tested using methods based on those derived by Magnusson and Kligman. Data were provided from a previously-conducted positive control study (Study No. GG6202) using 2-mercaptobenzothiazole.

No dermal irritation was observed 24 to 48 hours following the single challenge treatment with 30 or 75% ZA1296 to either previously-induced or control animals. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, **ZA1296 is not a dermal sensitizer.**

This study is classified as **acceptable (§81-6)** and satisfies the guideline requirement for a dermal sensitization study in the guinea pig.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: ZA1296
   Description: Light beige solid
   Lot/Batch #: P11, WRC 14845-32-2
   Purity: 95.1% (w/w)
   CAS #: Not provided

2. Vehicle and positive control: Deionized water.

   Positive control data from a previously-conducted study (Study No. GG6202) were provided using 2-mercaptobenzothiazole (purity not specified) in corn oil.

3. Test animals: Species: Guinea pig
   Strain: Hsd/Poc:DH albino
   Age: Young adult
   Weight: 423-605 g (all female; definitive study) and 452-574 g (all female; positive control study)
   Source: Harlan Porcellus Firgrove Farm, Heathfield, Sussex, UK
   Acclimation period: ≥6 Days
   Diet: RGP Diet (Labsure, Lavender Mill, Manea, Cambridgeshire, UK), ad libitum
   Water: Tap water, ad libitum
   Housing: One animal/cage in suspended stainless steel cages
   Environmental conditions:
   Temperature: 19±2 °C
   Humidity: 55±15%
   Air changes: Approximately 25-30 changes/hour
   Photoperiod: 12-Hour

B. STUDY DESIGN and METHODS:

1. In-life dates: August 1994 (definitive study)
   June - July 1994 (positive control study)

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Magnusson and Kligman [Magnusson, B. and Kligman, A.M., Allergic Contact Dermatitis in the Guinea Pig, Pub Thomas, (1970)]. Dose levels for the definitive study were based on the results of a sighting experiment [refer to page 12 of the study].

   For the induction treatment (definitive study), fur from the scapular area (approximately 5

x 5 cm) of 20 animals was clipped prior to the following six 0.05- to 0.1-mL injections: two injections of Freund's Complete Adjuvant:deionized water (1:1, v:v); two injections of 3% ZA1296 in deionized water (w:v); and two injections of 3% ZA1296 in Freund's Adjuvant:deionized water (1:1, v:v). Injections were made on each side of the mid-line. Test sites were observed for adverse effects on the following day. The second induction treatment was conducted 1 week following the intradermal treatment. The scapular area was again clipped, and a topical application (approx. 300 mg) of the test substance at 75% in deionized water (w:v) was applied to each animal via filter paper, which was held in place with tape covered by an adhesive bandage, and secured with PVC tape. This occlusive dressing was removed after 2 days and the site was examined approximately 1 day after removal. The 20 animals in the control group received similar inductions (intradermal injections and topical application) minus the test compound. The positive control induction phase was conducted using injections of a 3% (w:v) preparation of 2-mercaptobenzothiazole in corn oil, followed by topical application of a 75% dilution of this solution and, otherwise, the same manner as described.

Two weeks following the topical induction treatments, a single challenge exposure was conducted. For each animal, a 75% preparation of ZA1296 in deionized water (w:v; approximately 150 mg/animal) was applied to filter paper, which was then affixed to the top left shorn flank. On the bottom left shorn flank, approximately 0.1-0.2 mL of a 30% preparation of ZA1296 in deionized water was applied via filter paper. Similar applications were made to the right side of the animal using only deionized water. The occlusive dressing (filter paper stitched to rubber sheeting), covered with an adhesive bandage was removed after 24 hours. The positive control challenge phase was conducted using a 30% preparation of 2-mercaptobenzothiazole in corn oil (w:v) and, otherwise, in the same manner as previously described. Animals were observed for erythematous reactions according to the following scale 24 and 48 hours following patch removal:

0 - No erythema
1 - Scattered mild redness
2 - Moderate diffuse redness
3 - Intense redness and swelling

Body weights were recorded pretest and on study day 25.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: Induction reactions were not reported.

B. Challenge reactions and duration: No dermal irritation was observed 48 or 72 hours following administration of the single challenge treatment with 30 or 75% ZA1296 to either

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previously-induced or naive control animals. Based on the results of this study, ZA1296 is not a dermal sensitizer.

C. Positive control: Following challenge with 30% 2-mercaptobenzothiazole, mild to moderate redness (scores of 1-2) was observed in 19/20 treated animals. No adverse effects were observed in the controls. These data verify the adequacy of the test species and methods employed.

D. Deficiencies: Induction reactions were not reported, but should not affect the outcome of the study. No other deficiencies were noted.

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