DATA EVALUATION RECORD

MESOTRIONE (ZA1296) 7/19/2000

Study Type: §81-4, Primary Eye Irritation Study

Work Assignment No. 2-01-52I (MRID 44373518)

Prepared for
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Pesticide Health Effects Group
Sciences Division
Dynamac Corporation
2275 Research Boulevard
Rockville, MD 20850-3268

Primary Reviewer:
Kimberly S. Woodard, B.S.

Signature: Kimberly S. Woodard
Date: 12/13/99

Project Manager:
Mary L. Menetrez, Ph.D.

Signature: Mary L. Menetrez CEP
Date: 12-13-99

Disclaimer

This Data Evaluation Record may have been altered by the Health Effects Division subsequent to signing by Dynamac Corporation personnel.

David Nixon 7/11/2000

Mcopley 7/19/2000

EPA Reviewer: David Nixon, DVM
Registration Action Branch 1/HED (7509C)

Work Assignment Manager: Marion Copley, DVM
Registration Action Branch 1/HED (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS Number: 870.2400

OPP Guideline Number: §81-4

DP BARCODE: D259369
P.C. CODE: 122990

SUBMISSION CODE: S541375
TOX. CHEM. NO.: None

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

SYNONYMS: None specified.

CITATION: Robinson, P. (1994) ZA1296: eye irritation to the rabbit. Zeneca Central Toxicology Laboratory, Macclesfield, Cheshire, UK. Laboratory Report No. CTL/P/4505, Study No. FB4997. November 3, 1994. MRID 44373518. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, DE.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44373518), 100 mg of ZA1296 (95.1% purity) was instilled into the conjunctival sac of one eye of nine young adult New Zealand White female rabbits. Immediately following instillation, 3/9 treated eyes were flushed with 200 mL of water. The animals were observed for up to 4 days following instillation, and eye irritation was scored by the Draize method.

Very slight to slight conjunctival effects were observed in all treated unwashed eyes; however, only 2/6 animals exhibited positive ocular irritation, both at 1 hour following instillation: one animal exhibited moderate conjunctival redness, slight conjunctival chemosis, and moderate conjunctival discharge; the other animal exhibited transient slight corneal opacity affecting up to 25% of the total area and slight iritis. All positive ocular irritation (corneal, iridial, and conjunctival) subsided by 1 day, and all remaining slight conjunctival effects subsided by 4 days.

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In this study, **ZA1296 is a mild ocular irritant**, and is classified as **TOXICITY CATEGORY IV** for primary eye irritation based on the positive irritation observed in 2/6 treated unwashed eyes that subsided by day 1.

Since the test material was described only as a solid, and was not ground prior, this study is deemed **unacceptable (§81-4)** and does not currently satisfy the guideline requirement for a primary eye irritation study in the rabbit. This study may be upgraded to acceptable status if the study author provides information that the test material, as received, was suitable for use. Otherwise, additional data using ground test material and three additional animals are required.

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: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult
   Weight: 2799-3846 g (all female)
   Source: Charles River UK Ltd, Manston Road, Margate, Kent, UK
   Acclimation period: ≥6 Days
   Diet: Standard Rabbit Diet (STANDRABSQC), Special Diet Services, Witham, Essex, UK, ad libitum
   Water: Tap water, ad libitum
   Housing: One animal/cage in aluminum sheet cages
   Environmental conditions:
   Temperature: 17±2 °C
   Humidity: 55±15%
   Air changes: Approximately 25-30 changes/hour
   Photoperiod: 12-Hour light/dark

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B. STUDY DESIGN and METHODS:

1. In-life dates: July - August 1994

2. Animal assignment and treatment: A 100-mg portion of ZA1296 was instilled into the conjunctival sac of the left eye of six young adult New Zealand White female rabbits. The upper and lower lids were held together briefly before releasing to prevent loss of the material. The contralateral eye served as an untreated control. Immediately following application, the initial pain reaction of each rabbit was assessed. The animals were observed for ocular irritation at 1 hour, and 1, 2, 3, and when applicable, 4 days following instillation. Eye irritation was scored by the Draize method. At the day 1-4 observations, sodium fluorescein dye procedures were used to assess corneal damage. A modified Kay and Calandra system was used to interpret and classify numerical scores. Because irritation had not completely subsided by day 3, an additional three female rabbits were dosed in a similar manner, but the test eye was irrigated with 200 mL of clean luke warm water immediately following dosing. Body weights were recorded at day 1.

II. RESULTS AND DISCUSSION:

A. Clinical observations: The incidence of positive ocular irritation in treated unwashed eyes is presented in Table 1. Although very slight to slight ocular effects were observed in 6/6 treated eyes, only 2/6 animals exhibited positive ocular irritation, both at 1 hour following instillation: one animal exhibited moderate conjunctival redness (score of 2), slight conjunctival chemosis (score of 2), and moderate conjunctival discharge; the other animal exhibited transient slight corneal opacity (score of 1) affecting up to 25% of the total area (score of 1) and slight iritis (score of 1). All positive ocular irritation (corneal, iridial, and conjunctival) subsided by 1 day, and all remaining slight conjunctival effects subsided by 4 days. In this study, ZA1296 is a mild ocular irritant.

In comparison, 1/3 treated irrigated eyes exhibited positive ocular irritation, characterized by moderate conjunctival redness (score of 2) between 1 hour and 1 day. All positive irritation subsided by 2 days, and all remaining slight conjunctival effects subsided by 3 days. No corneal or iridial changes were observed.

Table 1. Incidence of positive ocular effects in unwashed treated eyes.

Observations	Number "Positive"/Number Tested				
	1 Hour	1 Day	2 Day	3 Day	4 Day
Cornea	1/6	---	---	---	---
Iris	1/6	---	---	---	---
Conjunctiva					
Redness	1/6	---	---	---	---
Chemosis	1/6	---	---	---	---
Discharge [a]	1/6	---	---	---	---

--- No positive observations.
a Discharge is not included in evaluating a positive reaction; however, scores of ≥2 are presented.

B. Deficiencies: Subdivision F guidelines state that solid test substances should be ground to a fine powder prior to use. In this study, the test material was described as a light beige solid, and the study author reported that in all cases, approximately 25% of the instilled material was immediately displaced. As a result, this study is deemed unacceptable and does not currently satisfy guideline requirements. This study may be upgraded to acceptable status if the study author provides information that the test material, as received, was suitable for use. Otherwise, additional data using ground test material and three additional animals are required.

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