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DATA EVALUATION RECORD

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

OPP Guideline Number: §81-4

DP BARCODE: D241232
P.C. CODE: 070705
EPA REG. NO.: 3125-LRE

SUBMISSION CODE: S534142
TOX. CHEM. NO.:

TEST MATERIAL (PURITY): KBR 3023 (96.7% purity)

SYNONYMS: 2-(2-Hydroxyethyl)-1-piperidinecarboxylic acid; 1-(1-methylpropoxycarbonyl)-2-(2-hydroxyethyl)piperidine; 1-methylpropyl 2-(2-hydroxyethyl)-1-piperidine-carboxylate

CITATION: Wakefield, A. (1997) Primary eye irritation study in rabbits with technical grade KBR 3023. Corning Hazleton, Inc., Vienna, VA. Laboratory Study Number 18202-0-820. April 24, 1997. MRID 44408710. Unpublished.

SPONSOR: Bayer Corporation, Agricultural Division, 17745 S. Metcalf, Stilwell, KS.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44408710), 0.1 mL of KBR 3023 (96.7% purity) was instilled into the conjunctival sac of the right eye of three adult New Zealand White rabbits/sex. The animals were observed for up to 14 days following instillation, and eye irritation was scored by the Draize scale.

Although ocular irritation was evident in all treated eyes within 1 hour of instillation, it was most severe between 24 and 48 hours, with average irritation scores of 27.5 and 21.5, respectively. Between 24 and 48 hours, irritation included scattered or diffuse to easily discernible corneal opacity affecting up to 100% of the total area in 6/6 eyes, iridial effects in 3/6 eyes, slight to moderate conjunctival redness in 6/6 eyes, and very slight to slight conjunctival chemosis in 6/6 eyes. Positive conjunctival effects subsided by 96 hours, and corneal and iridial changes subsided by 7 days.

In this study, **KBR 3023 is a moderate ocular irritant** and is classified as **TOXICITY CATEGORY III** for primary eye irritation based on the corneal, iridial, and positive

conjunctival effects which subsided from all treated eyes by day 7.

This study is classified **Acceptable (§870.2400)** and satisfies the guideline requirement for a primary eye irritation study in the rabbit.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: KBR 3023
   Description: Clear viscous liquid
   Lot/Batch #: 030693
   Purity: 96.7%
   pH: 8.61
   CAS #: 119515-38-7

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Adult
   Weight: 2.35-2.39 kg males; 2.27-3.33 kg females
   Source: Hazleton Research Products, Inc., Denver, PA
   Acclimation period: 7 Days
   Diet: PMI Feeds Certified Rabbit High Fiber Diet (#5325), *ad libitum* following a gradual increase
   Water: Tap water, *ad libitum*
   Housing: One animal per cage
   Environmental conditions:
   Temperature: 16-21 °C
   Humidity: 50 ± 10%
   Air changes: Not specified
   Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: December 17-31, 1996

2. Animal assignment and treatment: A 0.1 mL aliquot of KBR 3023 was instilled into

the lower conjunctival sac of the right eye of three adult New Zealand White rabbits/sex. The upper and lower lids were held together for 1 second before releasing to prevent loss of the material. The left eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24, 48, 72, and 96 hours and 7 and 14 days following instillation. Eye irritation was scored by the Draize Ocular Grading System. At the 24-hour and subsequent (when necessary) observation intervals, fluorescein dye was used to confirm the presence or absence of corneal ulceration. Following each fluorescein exam, the treated eyes were flushed with a 0.9% saline solution. The animals were also observed for signs of ill health at least once daily during the 14-day study.

II. RESULTS AND DISCUSSION:

A. Clinical observations: The incidence of positive ocular irritation is presented in Table 1. No abnormal clinical effects were reported.

Irritation was evident in all treated eyes within 1 hour of instillation and included iridial changes (scores of 1) in 2/6 eyes, and moderate conjunctival redness (scores of 2), slight to moderate conjunctival chemosis (scores of 2-3), and moderate to severe conjunctival discharge (scores of 2-3) in 6/6 eyes. Irritation was most severe between 24 and 48 hours, with average primary irritation scores of 27.5 and 21.5, respectively.

Between 24 and 48 hours, irritation included scattered or diffuse to easily discernible corneal opacity (scores of 1-2) affecting up to 100% of the total area (scores of 1-4) in 6/6 eyes, iridial effects (scores of 1) in 3/6 eyes, slight to moderate conjunctival redness (scores of 1-2) in 6/6 eyes, and very slight to slight conjunctival chemosis (scores of 1-2) in 6/6 eyes. Positive conjunctival effects subsided by 96 hours.

At 7 days, slight conjunctival redness (scores of 1) persisted in 4/6 eyes, though all corneal and iridial effects had subsided. No ocular irritation was evident after 14 days. In this study, KBR 3023 is a moderate ocular irritant.

TABLE 1. Incidence of Positive Ocular Effects

Observations	Number "Positive"/Number Tested						
	Hours					Days	
	1	24	48	72	96	7	14
Corneal Opacity	---	6/6	6/6	6/6	6/6	---	---
Iritis	2/6	3/6	3/6	1/6	1/6	---	---
Conjunctivae							
Redness	6/6	6/6	5/6	6/6	---	---	---
Chemosis	6/6	2/6	---	---	---	---	---
Discharge[a]	6/6	---	---	---	---	---	---

--- No positive observations.

[a] Discharge is not included in evaluating a positive reaction; however, scores of ≥ 2 are reported.

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