DATA EVALUATION REPORT

PEBULATE

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIGS (81-6)

Prepared for

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

4/13/1999

Prepared by

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DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea Pigs
OPPTS 870.2600 [§81-6]

DP BARCODE: D247841 SUBMISSION CODE: S546073
P.C. CODE: 041403 TOX. CHEM. NO.: 710
TEST MATERIAL (PURITY): Pebulate Technical (97.1%, a.i.)
SYNONYMS: Tillam
CITATION: Guest, R. (1990) Pebulate technical material: Magnusson & Kligman maximization study in the guinea pig. Safepharm Laboratories Limited, P.O. Box No. 45, Derby, DE1 2BT, U.K. CTL study no. GG4910, March 29, 1990. MRID 41614808. Unpublished.
SPONSOR: ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, SK10 4TJ.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 41614808) with Pebulate (97.1%), 30 young adult female Dunkin-Hartley guinea pigs were tested using the Magnusson & Kligman maximization test. Positive control was 2,4-dinitrochlorobenzene in corn oil.

The animals were shaved and intradermally induced with three pairs of injections: 1) 1:1 preparation of Freund's Complete Adjunct and corn oil; 2) 30% w/v test material in corn oil; and 3) 30% w/v test material in 1:1 preparation of Freund's Complete Adjuvant plus corn oil. One week later, the same area was clipped. The animals were topically induced with the undiluted test material (0.2-0.3 mL) and the dressing removed 48 hours later. Skin reactions were evaluated 1 and 24 hours following the dressing removal. The control animals were treated using the same procedures with the exception that no test material was used. Two weeks later and using the same technique as for the topical induction, the test and control animals were challenged with 0.1-0.2 mL of 10% w/v test material in corn oil on the right shorn flank and 3% w/v test material in corn oil on the left shorn flank. The dressing was removed after 24 hours. Twenty-four and 48 hours after patches were removed, the challenge site was scored for erythema and edema.

Dermal reactions after intradermal induction were not reported. After the second induction, scattered mild redness was noted on 19/20 and 6/20 sites at 1 and 24 hours after patch removal. An incidence of moderate and diffuse redness were noted at one hour after removal of patch. Also, small superficial scattered scabs were noted at 24-hour following the second induction. No dermal reactions were observed following challenge with the test material.

Under conditions of this study, Pebulate Technical was not a dermal sensitizer.

This study is classified as **Acceptable (guideline)** and satisfies the guideline requirement for a dermal sensitization study (81-6) 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: Pebulate Technical
   Description: clear, orange-colored liquid
   Lot/Batch #: CTL reference Y06381/001/007
   Purity: 97.1% a.i.

2. Vehicle and positive control
   Vehicle – corn oil
   Positive control – intradermal induction: 0.3% w/v 2,4-dinitrochlorobenzene in corn oil, topical induction: 3% w/v 2,4-dinitrochlorobenzene in corn oil, challenge: 0.3% w/v and 0.1% w/v 2,4-dinitrochlorobenzene in corn oil

3. Test animals
   Species: guinea pig
   Strain: Dunkin-Hartley
   Age and weight at start of treatment: ~8-10 weeks; 304-378 g
   Source: David Hall Limited, Burton-on-Trent, Staffordshire, U.K.
   Acclimation period: ≥5 days
   Diet: guinea pig FDI Diet, Special Diet Services Limited, Witham, Essex, U.K. *ad libitum*
   Water: tap water, *ad libitum*
   Housing: ≤3/polypropylene cages with solid-floor
   Environmental conditions:
   Temperature: 18-21°C
   Humidity: 45-66%
   Air changes: ~15/hour
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates
   Start: 01/25/90 End: 03/29/90

2. Animal assignment and treatment
   Preliminary studies were done with 6 animals to determine the concentrations to be used in the intradermal induction, topical induction, and challenge phase.

The test animals were induced and challenged according to the Magnusson & Kligman maximization test. An area approximately 40 mm X 60 mm on the shoulder region of 30 female guinea pigs was shaved. A row of three 0.1 mL injections was made on each side of the midline. The injections were: 1) 1:1 preparation of Freund's Complete Adjuvant plus corn oil; 2) 30% w/v test material in corn oil; and 3) 30% w/v test material in 1:1 preparation of Freund's Complete Adjuvant plus corn oil. One week later, the same area was clipped. The undiluted test material (0.2-0.3 mL) was applied on Whatman No. 4 filter paper which was held in place by a strip of surgical adhesive tape and covered with an overlapping length of aluminum foil. A strip of elastic adhesive bandage wound in a double layer around the torso of each animal. The dressing was removed 48 hours later. Skin reactions were evaluated 1 and 24 hours following the dressing removal. The control animals were treated using the same procedures with the exception that no test material used. Two weeks later, the flank area of each animal was clipped. Using a similar technique as with the topical induction, the test and control animals were challenged with 0.1-0.2 mL of 10% w/v test material in corn oil on the right shorn flank and 3% w/v test material in corn oil on the left shorn flank. The dressing was removed after 24 hours. Twenty-four and 48 hours after patches were removed, the challenge site was scored for erythema and edema.

Approximately one month earlier, a positive control study was done by the laboratory using the same procedures as the current study with the exception that the intradermal induction phase was with 0.3% w/v 2,4-dinitrochlorobenzene in corn oil, the topical induction phase was with 3% w/v in corn oil, and the challenge phase was with 0.3% w/v and 0.1% w/v in corn oil.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

Dermal reactions after intradermal induction were not reported. Scattered mild redness was noted on 19/20 and 6/20 sites at 1 and 24 hours after patch removal. Moderate and confluent redness was noted on one animal at one hour and small superficial scabs were noted at the 24-hour observation. The control animals had no reactions.

B. CHALLENGE REACTIONS AND DURATION

No reactions were noted on any animals following challenge. Pebulate Technical is not a sensitizer to the skin of female Hartley guinea pigs.

C. POSITIVE CONTROL

A sensitization rate of 100% was obtained with the positive control.

D. DEFICIENCIES

None

SignOff Date:	4/13/99
DP Barcode:	D254687
HED DOC Number:	013311
Toxicology Branch:	TOX1