UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

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JAN 31 1989

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Busan 11-M1 - Delayed Contact Hypersensitivity Study in Guinea Pigs; EPA File Symbol 1448-RNL; Busan 11-M3

TO: Larry Schnaubelt
Product Manager (21)
Registration Division (TS-767)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 1/26/89
Toxicology Branch II, Section II
Health Effects Division (TS-769C)

Thru: K. Clark Swentzel K. Clark Swentzel 1/27/89
Toxicology Branch II, Acting Head Section II
Health Effects Division (TS-769C)

and

Marcia van Gemert, Ph.D. Marcia van Gemert 1/30/89
Acting Chief, Toxicology Branch II/HFSA/HED(TS-769C)

Registrant: Buckman Laboratories International, Inc.
Chemical: Modified Barium Metaborate
Synonyms: Busan 11-M1
Project: 9-0434
Caswell No.: 71
Record No.: 235312

Action Requested: None.

Comment: The Registrant has submitted a guinea pig dermal sensitization study on Busan 11-M1 in support of both the Busan 11-M3 and Busan 11-M4 registrations. This study was submitted in response to an EPA request dated June 23, 1988. Toxicology Branch II files contain no information on any of these compounds. The revised label for Busan 11-M3 (modified barium metaborate), accompanying the study report, indicates that Busan 11-M3 contains 52% barium metaborate (active ingredient).

The study has been reviewed and the DER is attached.

Busan 11-M1 was tested at a concentration of 75% using an adaptation of the method of Pitt and Buehler. Under the conditions of the test, Busan 11-M1 was not shown to be a contact dermal sensitizer; however, since no positive control was tested and no data regarding historical positive control data were provided, the study is classified as Supplementary.

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Reviewed by: Linda L. Taylor, Ph.D. Linda Lee Taylor 1/24/89
Tox. Branch II, Section II (TS-769C)
Secondary Reviewer: K. Clark Swentzel K. Clark Swentzel 1/27/89
Acting Head, Section II, Tox. Branch II (TS-769C)

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization Study - Guinea Pigs

TOX CHEM NO: 71

MRID NO: 408984-01

TEST MATERIAL: Busan 11-M1; not otherwise identified

SYNONYMS: no information

STUDY NUMBER: 88-3288-21

SPONSOR: Buckman Laboratories International, Inc.

TESTING FACILITY: Hill Top Biolabs, Inc.

TITLE OF REPORT: Delayed Contact Hypersensitivity Study in Guinea Pigs

AUTHORS: James J. Kreuzmann, B.A.

REPORT ISSUED: October 1, 1988

CONCLUSION: Busan 11-M1 (75%-concentration in distilled water) did not show any response different from that of naive controls, under the conditions of the study. However, there was no positive control utilized in this study and no data were presented to show that a positive contact dermal sensitizer could be identified with the procedure utilized. Therefore, this study does not satisfy the requirement for this study type.

CLASSIFICATION: Core-Supplementary; no positive control was utilized and no historical control data regarding positive controls used at the testing facility were provided.

A. MATERIALS:

1. Test Compound: Busan 11-M1
   Description: a white powder
   Batch #: Lot # 8-11866
   Purity: not specified in report, but stated to be the responsibility of the sponsor.

   Note: Information on Busan 11-M1 could not be found in the Toxicology Branch files. It is assumed that Busan 11-M1 is a modified barium metaborate, possibly the technical grade.

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2. Test Animals:
   Species: guinea pigs
   Strain: Hartley albino
   Age: not specified
   Weight: 329-526 grams
   Source: Murphy Breeding Laboratories, Inc.

Study Design: The method used was an adaptation of the method of Ritz and Buehler (Fitz, H.L. and Buehler, E.V., Current Concepts in Cutaneous Toxicity, ed. Drill, V.A. and Lazar, P., Academic Press, 1980, pp 25-40). As stated in the protocol (not in the final report), the guinea pigs were chosen by size to fit the restraining device. Twenty test animals, 10 naive controls and 4 per pilot study were used.

Body weights were apparently obtained prior to the study and at termination, although there is no statement in the final report or the protocol about body-weight measurements. The final report presents a table of "Initial" and "Terminal" body weights for 48 animals. Ten of these were animals not used on the study. The 8 animals used in the primary irritation phase (pilot study) were not weighed at "termination".

Pilot Study: Bisan 11-M1 was tested at 0.5, 1.0, 2.5, 5.0, 10, 25, 50, and 75 % concentrations (w/v, in distilled water) to determine the appropriate concentrations to be used in the induction and challenge phases. Two males and 2 females were each treated with 10, 25, 50, and 75% concentrations (4 patch sites/animal), and 2/sex were treated at 0.5, 1.0, 2.5, and 5.0% concentrations.

The hair on the back of each animal was closely clipped one day prior to dermal application. Closed patches were applied in the following manner. Test article was applied in an appropriate volume into the selected patch system and the patches were applied to the clipped surface of the restrained animal. The patch was then occluded with a rubber dental dam pulled taut and fastened to the bottom of the restrainer. After approximately 6 hours, the dental dam and patches were removed, and the animals were put back into their cages. After 24 hours, the animals were depilitated and scored (0= no reaction - 3=severe erythema with or without edema).

a) induction phase - the left shoulder of each animal was clipped one day before exposure. Closed patches with test material (75%) were applied as in pilot study. This procedure was repeated at the same site once a week for the next 2 weeks (total of 3 six-hour exposures). After the last exposure period, the animals remained untreated for two weeks.

b) challenge phase - animals previously exposed during the induction phase, as well as the previously untreated controls, were challenged with the test material two weeks after the last application. The same procedure was used as above, except a skin site not previously exposed was used. One day after challenge, the animals were depilitated with a commercial depilatory (15 minute exposure followed by a wash with warm water). After 2 hours, the test sites were graded as before (reported as 24-hour scores). The grading was repeated the following day (reported as 48-hour scores).

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Note: Although the table on page 12 of the final report, which lists the number of animals used in the various phases of the study, indicates that 5 male and 5 female positive controls were to be used in the primary challenge phase, the protocol indicates the naive (5/sex) controls were used in the challenge phase. In Table 2 of the final report (page 17), the data presented are identified as the results in Test Material in Positive Control Animals. No positive control compound was identified in either the final report or the protocol.

Results: The only response observed in the induction phase of the study was slight patchy erythema (at 24 hours only), which was noted in one male at the lowest dose tested but not at the three higher doses to which he was exposed. All other males showed no reaction. One female tested at the 4 lowest dose levels showed slight patchy erythema at 5.0%. The two females exposed to the 4 highest levels both responded to the 75% concentration; one of these also responded at the 50% level and the other responded at the 25% level. No animal displayed edema at any time point.

Following the challenge exposure, fourteen out of 20 test material animals and 9 out of 10 naive controls displayed slight patchy erythema at the 24-hour scoring period. At 48 hours, 3 test material animals and 2 naive controls still displayed this response.

The body-weight gains were comparable between the naive controls and the test animals.

CONCLUSION: Busan 11-M1 did not show any response different from that of naive controls, under the conditions of the study. However, there was no positive control utilized in this study and no data were presented to show that a positive contact dermal sensitizer could be identified with the procedure utilized. Therefore, this study does not satisfy the requirement for this study type.