UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Suttocide A: Review of two dermal sensitization studies in human (patch test)

DP BARCODE: D213998 & D214000 **SUBMISSION CODE:** S480217
P.C. CODE: 128972 **TOX. CHEM. NO.:** Unknown
ID No. 057978-U & 057978-G **MRID No.:** 43514301

CHEMICAL (synonym): Sodium hydroxymethylamino acetate

TO: V. Goncarovs/M. Johnson, PM Team 31
Registration Division (7505C)

FROM: Whang Phang, Ph.D. 3/13/96
Pharmacologist
Tox. Branch II/ HED (7509C)

THROUGH: James Rowe, Ph.D. 3/13/96
Section Head, Section III
and
Stephanie Irene, Ph.D.
Acting Branch Chief
Tox. Branch II/ HED (7509C) 3/16/96

The registrant, Sutton Laboratories, Inc., submitted two dermal sensitization studies in human (patch tests) under a single MRID Number. These two studies have been reviewed, and the evaluations of these studies are presented in one DER, which is attached. The citations and the conclusions are presented below:

Shanahan, R.W. (1993) Suttocide A-Dermal toxicity data. Final report: Clinical safety evaluation: Suttocide A (at 0.5% aq.)-Repeated insult patch test, and Final report: Clinical safety evaluation: Suttocide A - 50% solution (Integra 44) - Repeated insult patch test of 1% active Suttocide A neutralized to Ph 7 with lactic acid. Essex Testing Clinic, Inc., Verona, NJ. Study No. 3106.01-02 and 3799.03. Jan. 17, 1993. Submitted to EPA by Sutton Labs., Inc.; MRID No.43514301

In two dermal sensitization studies (patch test) in human volunteers(MRID No.43514301), Suttocide A was tested in one study as a 0.5% aq. and in another as 1% a.i. in aqueous solution. The results indicated that Suttocide A was not considered to be a dermal sensitizer, under the conditions of these two studies.

In reply to your request in Bean Sheet, DP Barcode: 213998, these two studies are acceptable and fulfill the data requirements for a dermal sensitization study (81-6). It should be noted that a dermal sensitization study in guinea pigs with Suttocide A (5% aqueous solution) showed slight erythema in 6/10 amd mild erythema in 1/10 guinea pigs. In another dermal sensitization study in guinea pigs, 0.5% aqueous solution did not appear to cause dermal sensitization. Based on these data, Suttocide A at 5% or above may produce dermal sensitization.

EPA Reviewer: Whang Phang, Ph.D. Whang 3/12/96
Review Section III
Toxicology Branch II (7509C)

EPA Secondary Reviewer: Steven Malish, Ph. D. S.2.Malish 3/12/96
Review Section III
Toxicology Branch II (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Dermal sensitization study - human (2 studies)
OPPTS 870.2600 [§81-6]

DP BARCODE: D214000 **SUBMISSION CODE:** S480217
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ID No. 057978-U **MRID No.:** 43514301

CHEMICAL: Sodium hydroxymethylamino acetate

SYNONYMS: Suttocide A

CITATION: Shanahan, R.W. (1993) Suttocide A-Dermal toxicity data. Final report: Clinical safety evaluation: Suttocide A (at 0.5% aq.)-Repeated insult patch test, and Final report: Clinical safety evaluation: Suttocide A - 50% solution (Integra 44) - Repeated insult patch test of 1% active Suttocide A neutralized to pH 7 with lactic acid. Essex Testing Clinic, Inc., Verona, NJ. Study No. 3106.01-02 and 3799.03. Jan. 17, 1993. Submitted to EPA by Sutton Labs., Inc.; MRID No.43514301

SPONSOR: Sutton Laboratories, Inc.

EXECUTIVE SUMMARY: In two dermal sensitization studies (patch test) in human volunteers (MRID No.43514301), Suttocide A was tested in one study as a 0.5% and in another as 1% a.i. in aqueous solution. The results indicated that Suttocide A, under the conditions of these two studies, was not considered to be a dermal sensitizer.

These two studies are acceptable and fulfill the data requirements for a dermal sensitization study (81-6).

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements are signed and are included in the report. A Flagging statements is not provided, but it is not necessary for this study because data do not meet the criteria for flagging.

I. MATERIALS AND METHODS

A. MATERIALS:

Study 1: Suttocide A-Dermal toxicity data. Final report: Clinical safety evaluation: Suttocide A (at 0.5% aq.)-Repeated insult patch test. Suttocide A was neutralized to pH 7 with lactic acid.

1. Test Material: Suttocide A (0.5% in H_2O)
   Description: clear liquid
   Lot #: OBT-57
   Purity: not given
   Concentration: 0.5% w/v in distilled, deionized H_2O

2. Vehicle: distilled, deionzed water
   The control group received distilled, deionized water.

Study 2: Final report: Clinical safety evaluation: Suttocide A - 50% solution (Integra 44) - Repeated insult patch test of 1% active Suttocide A neutralized to pH 7 with lactic acid.

1. Test Material: Suttocide A (50% solution in distilled deionized water).
   Description: clear liquid
   Lot #: AS-135
   Purity: not given
   Concentration of the test solution: 2% aqueous solution (aq.) (1% a.i.)

2. Vehicle: distilled, deionzed water
   No vehicle control group was conducted.

3. Test subjects: Human volunteers

   For study No 1: 19 males and 87 females, ranging in age from 16 to 66 years. The test subjects did not exhibit any physical or dermatological conditions which would preclude them from the study.

   For study No 2: 42 males and 170 females, ranging in age from 18 to 64 years. The test subjects did not exhibit any physical or dermatological conditions which would preclude them from the study.

B. STUDY DESIGN and METHODS:

1. In life dates - Study No. 1: 9/24/90 to 11/2/90

Study No. 2: 4/21/93 to 6/21/93

2. Study design

a. Induction phase

Study 1

An application site on the upper left scapular area of the back was clean with 70% isopropyl alcohol prior to each patch application. Approximately 0.3 ml of 0.5% aq. test material was placed onto a 2 cm^2 Parke-Davis Readi-Bandage^R occlusive patch, which was then placed on the application site. The test subjects were instructed to remove the patch 24 hours (hrs) after application. The subjects were treated every Monday, Wednesday, and Friday until 9 applications were carried out. The application site was examined by the testing laboratory and scored prior to the nest patch application according to the following scale:

0 = No visible reaction
+ = Faint, minimal reaction
1+ = Erythema
2+ = Erythema, induration
3+ = Erythema, induration, vesicles
4+ = Severe reaction with Erythema, induration, vesicles pustules
E = Induration or other dermal sequelae recorded as mild, moderate or severe

If a test subject showed a dermal response of 2+ or greater during the induction phase, the next application site would be changed to a new area. If a 2+ or greater response still occurred on the new site, no further application would be carried out on this subject during the induction phase. However, this reactive subject would continue onto the challenge phase of the study.

Study No. 2

The experimental procedures were similar to those for Study No.

1 except that 0.3 ml of a 2% aq. (1% a.i.) was applied on each patch. For this study the scoring scales for dermal response in both induction and challenge phases are excerpted from the report and presented below:

0 = No evidence of any effect
+ = Barely perceptible (minimal, faint, uniform or spotty erythema)
1 = Mild (pink, uniform erythema covering of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (bright-red erythema with/without petechiae or papules)
4 = Severe (deep-red erythema with/without vesiculation or weeping)

b. Challenge phase

Study No. 1

After the last induction dose, there was a rest period of approximately 2 weeks when no treatment took place. Subsequently, the test subjects returned to the clinic, and the application sites for the Induction phase were examined and scored if there was any dermal response. The test subjects were also queried if there was any dermal response during the rest period. A challenge patch containing 0.3 ml ofa 0.5% test solution was applied to a naive site at the upper right scapular area of the back. The application sites were then examined and scored at 24, 48, and 72 hrs after application. The skin response scoring scale was similar to that presented above (Study No.1).

Study No. 2

The experimental procedures for Study No. 2 are similar to those of Study No. 1 except each challenge patch containing 0.3 ml of a 2 % test soluion was applied.

II. RESULTS AND DISCUSSION:

Study No. 1: Four test subjects were unable to complete the study for personal reasons, and they were discounted from the final analysis. A faint, minimal, and transient response (+) was seen in 1/102 subjects during the induction phase, and no response was observed in this individual during the challenge phase. During the challenge phase only 1/102 test subject showed a faint, minimal, and transient response (+) which was not seen during the induction phase. In a vehicle control subject, a faint, minimal, and transient dermal response (+) was also seen during the challenge phase. **Based on these observations, the test material (at 0.5% aq) was not considered to be a dermal sensitizer under the conditions of this study.**

Study No. 2: In this study, 201/212 completed the study. Ten test subjects discontinued the study due to personal reasons, and one subject violated the study protocol and was dropped from the study. In this study, the 48 hr reading was inadvertantly omitted for 53 subjects. One test subject showed signs of barely perceptible to mild reponse (+ to 1+) during the induction phase (Exposure No. 3 to 6) and of barely perceptible response (+) at the the challenge phase (72 and 96 hrs). Furthermore, for this subject an additional 96 hr reading was included, and a faint response (+) was recorded at this reading. But dermal response did not persist during the induction phase (seen in 4 different examination periods). **Under the conditions of this study, the test article (50% , Integra^{R} 44; tested as a 1% a.i. aq) was not considered to be a dermal sensitizer.**

E. Deficiencies - No significant deficiencies, which would interfere with the interpretation of the test results, were found.