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DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization - Guinea Pig (81-6).

TOX. CHEM. NO.: 510A

ACCESSION NUMBER/MRID NO.: 410137-07

TEST MATERIAL: Chlorpropham Technical (SX-1817)

STUDY NUMBER(S): CEHC 2997

LABORATORY PROJECT I.D.: S-3177

SPONSOR: Chevron Chemical Company, Ortho Agricultural Chemicals Division, 15049 San Pablo Avenue, Richmond, California

TESTING FACILITY: Chevron Environmental Health Center, Inc., 15299 San Pablo Avenue, Richmond, California

TITLE OF REPORT: Modified Buehler Test for the Skin Sensitization Potential of Chlorpropham Technical

AUTHOR(S): K.K. Dougherty

REPORT ISSUED: February 16, 1989

CONCLUSION: Chlorpropham was tested for skin sensitizing potential in Guinea Pigs using a modified Buehler test. The levels tested were 75% and 5% Chlorpropham in ethanol (induction) and acetone (challenge). There were no sensitization responses in either of the treated groups. In the positive control group (DNCB), 10/10 animals showed a sensitization response. The test substance is not considered to be a sensitizer under the conditions of the study.

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: 1-methylethyl 3-chlorocarbanilate

Description: honey colored crystalline solid
Batch #(s), Other #(s): SX-1817
Purity: 99.9%
Source: Chevron Chemical Company
Vehicle: ethanol and acetone (challenge phase)
Positive Control: 1-chloro-2,4-dinitrobenzene (DNCB)

2. Test Animals:

Species and Strain (sexes): Male Hartley albino guinea pigs
Age: 48 day
Weight(s): 371-508 grams
Source(s): Charles River Breeding Laboratory, Portage, Michigan

3. Procedure:

a. Preparation and Analyses of Dosing Mixtures: The test chemical was diluted ethanol to either 75% or 5% (w/w) each dosing day. For the challenge doses, it was diluted to 75% (w/w) with acetone. The positive control, DNCB was dissolved w/w in 80% ethanol or acetone to 0.1% each dosing day. Samples for stability and homogeneity studies were taken at various times.

b. Protocol: Pre-test screens were conducted to determine the dose level which would induce minimal irritation and the dose level which would induce minimal to slight irritation. The dose levels selected were 75% and 5% dilutions.

Induction Phase: Fifteen animals were used for each of the two treated groups. Ten animals were used per group for the irritation and positive controls. The right flank of each animal was clipped the day before the start of the study and was reclipped throughout the study at weekly intervals. The first induction application consisted of 0.3 ml of the dosing mixture held in place by a Hill Top Chamber wrapped with a PEG bandage and secured with porous tape. The exposure period was 6 hours at which time the wraps were removed and the test material was wiped off the skin with a gauze pad. For the remaining induction applications, 0.4 ml of the test material was applied with a one-inch square gauze. The gauze was occluded with a 2-inch square of polyethylene and wrapped for 6 hours. The dosing schedule consisted of 10 applications administered on alternate days (Monday, Wednesday, Friday) over a 22-day period. Blind skin irritation readings were made 24 and 48 hours after the first induction application. Readings were also conducted 24 hours after the fifth and tenth induction applications to assess skin irritation resulting from repeated exposures. Skin irritation was evaluated using a modification of the Draize scoring system.

Challenge Phase: The animals were challenged 14 days after the tenth induction phase application. A clipped left flank was used for the challenge. A Hill Top Chamber containing 0.3 ml of the dosing mixture was applied and wrapped as in the induction phase. Blind scorings were conducted 24, 48, and 72 hours after dosing.

Assessment of Skin Irritation and Sensitization Potential: The following guideline was used for assessing skin irritation and sensitization potential: the skin irritation

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scores of the test animals were compared with their corresponding irritation controls. An animal was considered to be sensitized if its challenge irritation scores were greater and/or more persistent than (a) scores for animals in the same group following the initial induction application and (b) scores for animals in the corresponding irritation control group following a first exposure to (challenge with) the test material. Any skin reactions considered to be sensitization reactions after the first challenge were confirmed in a rechallenge.

c. Bodyweights: All animals were weighed on day 0, 24 hours following the tenth induction application, and on the last day of scoring for challenge.

d. Statistical Analyses: Body weights were statistically analyzed using one-way analysis of variance.

B. RESULTS:

Analyses of Dosing Solutions: The homogeneity and stability analyses indicated that the dosing mixtures were stable and that they were homogeneously mixed. Concentration check samples taken at challenge were found to contain 100% of target.

Summary of Irritation and Sensitization Results: The following table summarizes the irritation and sensitization results for this study. The table is taken from the text of the report.

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Summary of Incidence and Response and Mean Irritation Scores From Guinea Pigs Following Initial Dosing and Challenge Treatments With Chlorpropham Technical (SX-1817)

Dose Group	Incidence[a]	Mean Score[b] After Initial Treatment 24 hr.	48 hr.	Mean Score[b] After Challenge 24 hr.	48 hr.	72 hr.
Chlorpropham Technical High Dose[c]	0/15	0.3	0.2	0.6	0.1	0.1
Chlorpropham Technical Low Dose[d]	0/15	0.0	0.1	0.8	0.4	0.3
Chlorpropham Technical Irritation Control[e]	---	0.0	0.1	1.7	1.0	0.7
DNCB Positive Control[f]	10/10	0.2	0.8	3.8	3.4	2.9
DNCB Irritation Control[g]	---	0.0	0.0	0.4	0.2	0.1

a) Number of animals sensitized/number of animals tested.
b) Mean of the sum of Draize scores for erythema and edema.
c) Induced with 75% Chlorpropham Technical w/w in ethanol and challenged with 75% Chlorpropham Technical w/w in acetone.
d) Induced with 5% Chlorpropham Technical w/w in ethanol and challenged with 5% Chlorpropham Technical w/w in acetone.
e) Induced with 100% ethanol, challenged with 75% Chlorporpham Technical w/w in acetone.
f) Incuced with 0.1% DNCB w/w in 80% ethanol (v/v in distilled water) and challenged with 0.1% DNCB w/w in acetone.
g) Induced with 80% ethanol v/v in distilled water and challenged with 0.1% DNCB w/w in acetone.

There were no sensitization responses in either of the treated groups. In the positive control group, 10/10 animals showed a sensitization response. The test substance is not considered to be a sensitizer under the conditions of the study.

Bodyweights: No treatment-related changes were observed.

Quality Assurance Measures: Signed Good Laboratory Practice Statement and Quality Assurance Statements were provided.

C. DISCUSSION: This is an acceptable study and is classified as Core Guideline. Chlorpropham is not a sensitizer under the conditions of the study. The results show that there may be some "skin fatigue" following

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repeated doses of the test material since there were increased observations of irritation after 5 and after 10 treatments in the induction phase.

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