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

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MEMORANDUM

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: 239-2591, 239-2593. Chlorpropham. Review of Acute Toxicity  
Studies Received in Response to Registration Standard

Tox. Chem. No. 510A  
Project No. 9-1060

TO: Robert Taylor, PM #25  
Registration Division (H7505C)

FROM: Pamela M. Hurley Ph.D., Toxicologist *Pamela M. Hurley 11/8/89*  
Section I, Toxicology Branch I  
Insecticide, Rodenticide Support  
Health Effects Division (H7509C)

THRU: Roger L. Gardner, Acting Section Head *Roger Gardner 11-8-89*  
Section I, Toxicology Branch I  
Insecticide, Rodenticide Support  
Health Effects Division (H7509C)

Record No(s). 241621, 241622

Background and Request:

Valent Corporation has submitted five acute toxicity studies conducted on Technical Chlorpropham in response to the Registration Standard on Chlorpropham. The Toxicology Branch (TB-I) has been asked to review and comment upon the submitted toxicity studies.

Toxicology Branch Response:

TB-I has reviewed the submitted acute toxicity studies on Technical Chlorpropham and has determined that the studies are acceptable as fulfilling the regulatory requirements for Chlorpropham. The studies are all classified as Core Guideline and are summarized on the following page.

*[Handwritten signature]*

Studies Reviewed

.....Technical.....

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<u>Study</u>	<u>Results</u>	<u>Core Classification</u>
Acute oral LD <sub>50</sub> - rat	LD <sub>50</sub> 's: 4.1 (0.0-7.0) g/kg (M); 4.8 (2.9-7.1) g/kg (F)	Guideline
Acute dermal LD <sub>50</sub> - rabbit	LD <sub>50</sub> > 5.0 g/kg (both sexes)	Guideline
Primary Eye Irritation - rabbit	Mean irritation score 2.7 Minimally irritating	Guideline
Primary Dermal Irritation - rabbit	Primary dermal irritation score 0.3. Minimally irritating	Guideline
Dermal Sensiti- zation - G. Pigs	Not a sensitizer under conditions of study	Guideline

EPA Accession No. \_\_\_\_\_ Results: \_\_\_\_\_ Doc. No. \_\_\_\_\_

Study/Lab/Study #/Date	Material	EPA Accession No.	LD50, LC50, PIS, NOFL, LFL	Category	Guideline
acute oral LD <sub>50</sub> - rat/Chevron/CEHC 2993 February 16, 1989	Chlorpropham Technical SX-1817 99.97% pure	410137-03	LD <sub>50</sub> 4.1 (6.0-7.0) g/kg (M) 4.8 (2.9-7.1) g/kg (F)	III	Guideline
acute dermal LD <sub>50</sub> - rabbit/Chevron/ CEHC 2994 / February 8, 1989	"	410137-04	LD <sub>50</sub> > 5.0 g/kg	IV	Guideline
irritant Eye Irritation - Rabbit/Chevron/ CEHC 2995/January 27, 1989	"	410137-05	PIS = 2.7. Minimally irritating.	III	Guideline
irritant Dermal Irritation - Rabbit/ Chevron/CEHC 2996/January 26, 1989	"	410137-06	PIS = 0.3. Minimally irritating	IV	Guideline
dermal Sensitization - Guinea Pig/ Chevron/CEHC 2997/February 16, 1989	"	410137-07	NOT a sensitizer under conditions of study	N/A	Guideline

Reviewed By: Pamela Hurley, Ph.D. *P. Hurley 11/8/89*  
Section I, Tox. Branch, IRS (H7509C)  
Secondary Reviewer: Roger L. Gardner *Roger Gardner 11-8-81*  
Section I, Tox. Branch, IRS (H7509C)

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DATA EVALUATION REPORT

STUDY TYPE: Acute oral toxicity - rat (81-1)

TOX. CHEM. NO.: 510A

ACCESSION NUMBER/MRID NO.: 410137-03

TEST MATERIAL: Chlorpropham Technical (SX-1817)

STUDY NUMBER(S): CEHC 2993

LABORATORY PROJECT I.D.: S-3173

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: The Acute Oral Toxicity of Chlorpropham Technical (SX-1817)  
in Adult Male and Female Rats

AUTHOR(S): K.K. Dougherty

REPORT ISSUED: February 16, 1989

CONCLUSION: Technical Chlorpropham was tested in an acute oral toxicity study  
in male and female rats. 3.3, 4.6 and 6.5 g/kg were tested. The  
LD<sub>50</sub>'s were as follows: 4.1 (0.0-7.0) g/kg for males and 4.8  
(2.9-7.1) g/kg for females. The slope and 95% confidence limits  
were 5.7 (0.3-11.7) for males and 13.7 (1.9-25.4) for females.

Toxicity Category: III

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: 1-methylethyl 3-chlorocarbamate

Description: micronized white powder

Batch #(s), Other #(s): SX-1817

Purity: 99.9%

Source: Chevron Chemical Company

Vehicle (if applicable): Peanut oil

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2. Test Animals:

Species and Strain (sexes): Male and female Sprague-Dawley  
Cr1:CD<sup>®</sup>BR rats  
Age: 76 days (M), 81 days (F)  
Weight(s): 257-314 g (M), 198-243 g (F)  
Source(s): Charles River Laboratories, Inc., Portage, Michigan

3. Procedure:

a. Preparation of Dosing Mixtures: The test material was diluted in peanut oil at concentrations of 330, 460, and 650 mg/ml on the day of dosing. The mixtures were heated to approximately 40°C to facilitate mixing. The temperature was maintained during dosing.

Homogeneity Analyses: Homogeneity was assessed during the range finding study. Six samples each of freshly prepared low- and high dose solutions (50 and 650 mg/ml) were analyzed.

b. Basis For Selection of Dose Levels: Not directly stated, however, it appears that a range-finding study may have been conducted.

c. Animal Assignment and Dose Levels:

Test Group	Dose Admin- istered g/kg	Volume Administered		Number of Animals	
		male	female	male	female
Contr.	0	10 ml/kg	10 ml/kg	5	5
1	3.3	2.9 ml	2.2-2.3 ml	5	5
2	4.6	2.9 ml	2.2-2.3 ml	5	5
3	6.5	2.9 ml	2.2-2.3 ml	5	5

d. Clinical Observations and Mortality: The animals were observed frequently during the day of dosing for clinical signs of toxicity and for mortality and then once daily thereafter for 14 days.

e. Body Weight Determinations: The animals were weighed immediately before dosing and at 2, 7 and 14 days after treatment.

f. Gross Necropsy: A gross necropsy was conducted on all animals.

g. Histopathology: Abnormal tissues were collected and prepared for microscopic examination.

h. Statistical Analyses: The LD<sub>50</sub>, slope, and 95% confidence limits were determined using the method of Berkson. The mean body weights were compared between groups with three or more survivors using one-way analysis of variance.

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B. RESULTS:

1. Dosage Preparation: The dosing mixtures were determined to be homogeneous. For the 50 mg/ml concentration, the mean concentration observed for 6 samples was 55.3 mg/g (target concentration, 54.0 mg/g) or 102% of target. For the 650 mg/ml concentration, the mean concentration observed for 6 samples was 646 mg/g or 99.5% of the target concentration.
2. Clinical Observations and Mortality: All deaths occurred within four days after dosing. At the highest dose level, all the females died and 4/5 males died. The LD<sub>50</sub>'s were as follows: 4.1 (0.0-7.0) g/kg for males and 4.8 (2.9-7.1) g/kg for females. The slope and 95% confidence limits were 5.7 (0.3-11.7) for males and 13.7 (1.9-25.4) for females. The authors stated that the following clinical signs of toxicity were frequently observed: decreased motor activity, ataxia, hypothermia, reduced food consumption, yellow or brown anogenital discharge, tremors, abnormal respiratory sounds, and collapse. They also stated that the following signs were observed infrequently: convulsions, salivation, lacrimation, red ocular or nasal discharge, and diarrhea. With one exception of a female dosed with 4.6 g/kg, survivors were normal by day 4.
3. Body Weight Determinations: No treatment-related differences were observed. However, it should be noted that these were comparisons made between surviving groups of 3 or more.
4. Gross Pathology: Discolored lungs and vascularization in the cecum were observed.
5. Histopathology: No treatment-related lesions were observed.
6. Quality Assurance Measures: A signed quality assurance statement was provided.

C. DISCUSSION: This study is an acceptable acute oral study in rats. The LD<sub>50</sub>'s were as follows: 4.1 (0.0-7.0) g/kg for males and 4.8 (2.9-7.1) g/kg for females. The slope and 95% confidence limits were 5.7 (0.3-11.7) for males and 13.7 (1.9-25.4) for females. The study is classified as Core Guideline.

Reviewed By: Pamela Hurley, Ph.D. *P Hurley 11/8/89*  
Section I, Tox. Branch, IRS (H7509C)  
Secondary Reviewer: Roger L. Gardner *Roger Gardner 11-8-89*  
Section I, Tox. Branch, IRS (H7509C)

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DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal Toxicity - rabbit (81-2)

TOX. CHEM. NO.: 510A

ACCESSION NUMBER/MRID NO.: 410137-04

TEST MATERIAL: Chlorpropham Technical (SX-1817)

STUDY NUMBER(S): CEHC 2994

LABORATORY PROJECT I.D.: S-3174

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: The Acute Dermal Toxicity of Chlorpropham Technical (SX-  
1817) in Adult Male and Female Rabbits

AUTHOR(S): K.K. Dougherty

REPORT ISSUED: February 8, 1989

CONCLUSION: Technical Chlorpropham was tested in an acute dermal toxicity  
study in male and female rabbits using a single dermal application  
of 5.0 g/kg (limit test). The acute dermal LD<sub>50</sub> was greater than  
5.0 g/kg.

Toxicity Category: IV

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: 1-methylethyl 3-chlorocarbanilate

Description: micronized white powder

Batch #(s), Other #(s): SX-1817

Purity: 99.9%

Source: Chevron Chemical Company

Vehicle (if applicable): Physiological saline

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2. Test Animals:

Species and Strain (sexes): Young adult male and female New Zealand White rabbits

Age: 15-17 weeks

Weight(s): 2.80-3.01 kg (M), 2.83-3.11 kg (F)

Source(s): R and R Rabbitry, Stanwood, Washington

3. Procedure:

- a. Preparation of Animals and Dosing Mixtures: The test material was mixed 1:1 with physiological saline immediately prior to dosing. The fur on the trunks of 5 animals/sex was clipped the day before dosing. Five grams/kg of the test material was applied to the trunk of each animal and covered with gauze patches secured by porous tape. The trunk of each animal was then wrapped with a sheet of plastic film and paper toweling. The animals were fitted with plastic collars. After a 24 hour exposure period, the wrappings were removed and the remaining test material was wiped off using gauze pads and mineral oil. The collars remained on the animals an additional 24 hours. The skin at the application site was scored for irritation at 1, 7 and 14 days after treatment using the Draize method.
- b. Clinical Observations and Mortality: The animals were observed frequently for clinical signs of toxicity and for mortality on the first day after treatment and at least once daily for 14 days after treatment.
- c. Bodyweights: The animals were weighed immediately before dosing and at 2, 7, and 14 days after treatment.
- d. Gross Necropsy: A complete gross examination was conducted on all animals.
- e. Histopathology: Sections of skin from each animal were collected and preserved for possible microscopic examination.

B. RESULTS:

1. Clinical Signs of Toxicity and Mortality: No animals died during the study. Reduced food intake was observed on day 2 with 2 animals of each sex. The authors stated that this was probably due to the wrapping procedure. No other clinical signs of toxicity were observed. All animals showed well-defined erythema with slight edema (some animals) one hour after unwrapping. Slight erythema was observed on day 7. Except for some flakiness, the irritation cleared by day 14.
2. Body weight: Slight decreases in mean body weight were observed on day 2. By day 7, the animals had recovered and gained weight through day 14. The authors stated that early weight loss is

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common in animals dosed by this method and was probably not compound-related.

3. Gross Pathology: Two females showed flaky skin at necropsy. No other abnormalities were observed.
4. Histopathology: Not conducted.
5. Quality Assurance Measures: Signed Good Laboratory Practice Statement and Quality Assurance Statements were provided.

C. DISCUSSION: This was a limit test. The acute dermal LD<sub>50</sub> was greater than 5.0 g/kg. The study is Core Guideline and the toxicity category is IV.

Reviewed By: Pamela Hurley, Ph.D. *P Hurley 11/8/89*  
Section I, Tox. Branch, IRS (H7509C) *Roger Gardner 11-8-89*  
Secondary Reviewer: Roger L. Gardner  
Section I, Tox. Branch, IRS (H7509C)

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DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation - rabbit (81-4)

TOX. CHEM. NO.: 510A

ACCESSION NUMBER/MRID NO.: 410137-05

TEST MATERIAL: Chlorpropham Technical (SX-1817)

STUDY NUMBER(S): CEHC 2995

LABORATORY PROJECT I.D.: S-3175

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: The Acute Eye Irritation Potential of Chlorpropham Technical  
(SX-1817) in Adult Albino Rabbits

AUTHOR(S): K.K. Dougherty

REPORT ISSUED: January 27, 1989

CONCLUSION: Technical Chlorpropham was tested in a primary eye irritation  
study in rabbits. One-tenth milliliter was tested on each rabbit.  
The mean primary eye irritation score was 2.7, corresponding to a  
rating of minimally irritating.

Toxicity Category: III

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: 1-methylethyl 3-chlorocarbanilate

Description: micronized white powder

Batch #(s), Other #(s): SX-1817

Purity: Not given

Source: Chevron Chemical Company

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2. Test Animals:

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Species and Strain (sexes): Young adult New Zealand White rabbits

Age: 13-15 weeks and 7-8 months

Weight(s): Not given

Source(s): R and R Rabbitry, Stanwood, Washington

3. Procedure:

One-tenth milliliter of the test material was placed in the conjunctival sac of one eye of each of 9 rabbits. After a 30-second exposure, both eyes of 3 of the rabbits were then rinsed with distilled water for 1 minute at a rate of 250 milliliters/minute. Reported control eyes were taken from the animals that were rinsed. All the eyes were examined for ocular irritation at 1, 24, 48, and 72 hours after treatment and graded according to the method of Draize.

All animals were examined once daily for clinical signs of toxicity. At the end of the study, all animals were examined externally and then sacrificed.

B. RESULTS:

Treated Unrinsed Eyes: No effects on either the cornea or the iris were observed. Slight to moderate conjunctival redness was observed in 5/6 animals 1 hour after treatment. By 24 hours, only slight redness was observed in 2 animals. At 48 hours, this redness was found in one animal and at 72 hours, no effects remained on any of the rabbits. Slight chemosis was observed in one animal at 1 hour. This had disappeared by 24 hours. The highest mean irritation score was 2.7 at 1 hour. This corresponds to a classification of minimally irritating.

Treated Rinsed Eyes: No effects were observed on either the cornea or the iris. Slight to moderate conjunctival redness was observed in 3 rabbits at 1 hour. At 24 and 48 hours, slight redness was observed in one animal. This had cleared by 72 hours. The highest mean irritation score was 3.3 at 1 hour. This corresponds to a classification of minimally irritating. In 3 control eyes, slight to moderate conjunctival redness was observed at 1 hour. This disappeared by 24 hours. The mean irritation score was identical to that of the treated animals.

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

C. DISCUSSION: It is interesting to note that the score for the control eyes was identical to that for the rinsed animals (slightly higher than unrinsed animals, probably due to the smaller number of animals tested). This is an acceptable study and the classification is Core Guideline. The mean irritation score for unrinsed eyes is 2.7, corresponding to a classification of minimally irritating.

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Secondary Reviewer: Roger L. Gardner *Roger Gardner 11-8-89*  
Section I, Tox. Branch, IRS (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation - rabbit (81-5)

TOX. CHEM. NO.: 510A

ACCESSION NUMBER/MRID NO.: 410137-06

TEST MATERIAL: Chlorpropham Technical (SX-1817)

STUDY NUMBER(S): CEHC 2996

LABORATORY PROJECT I.D.: S-3176

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: The Four-Hour Skin Irritation Potential of Chlorpropham  
Technical (SX-1817) in Adult Albino Rabbits

AUTHOR(S): K.K. Dougherty

REPORT ISSUED: January 26, 1989

CONCLUSION: Technical Chlorpropham was tested in a primary dermal irritation  
study in rabbits. One-half gram was tested on each rabbit,  
abraded and unabraded. The primary dermal irritation score was  
0.3. The test material is considered to be minimally irritating.

Toxicity Category: IV

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: 1-methylethyl 3-chlorocarbamate

Description: micronized white powder

Batch #(s), Other #(s): SX-1817

Purity: 99.9%

Source: Chevron Chemical Company

Vehicle (if applicable): Physiological saline

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2. Test Animals:

Species and Strain (sexes): Young adult New Zealand White rabbits

Age: 15-17 weeks

Weight(s): Not given

Source(s): R and R Rabbitry, Stanwood, Washington

3. Procedure:

- a. Preparation of Animals and Dosing Mixtures: The test material was mixed 1:1 with physiological saline prior to dosing. The fur on the trunks of 6 animals was clipped the day before dosing. One-half gram of the test material was applied to two test sites/animal, one intact and one abraded. One-half milliliter of physiological saline was added to each treated site by syringe after application of the test material to insure better contact with the skin. The test sites were then covered with gauze patches secured by porous tape. The trunk of each animal was then wrapped with a sheet of plastic film and paper toweling. The animals were fitted with plastic collars. After a 4 hour exposure period, the wrappings and collars were removed and the remaining test material was wiped off using gauze pads and mineral oil. The skin at the application site was scored for irritation at 1, 24, 48 and 72 hours, and at 7 and 14 days after treatment using the Draize method.
- b. Gross Necropsy: An external examination was conducted on all animals.
- c. Histopathology: Sections of skin sites with irritation or injury persisting to day 14 were collected and preserved for possible microscopic examination.

B. RESULTS:

1. Skin Irritation: The Primary Irritation Score (PIS) for the test material was 0.3. The test material caused slight erythema with no edema through day 7 (one animal on day 7 had minimal erythema). The erythema had completely disappeared by 72 hours in all animals but reappeared in one animal on day 7. Dry and flaky skin appeared on all animals at day 7 and was observed on both intact and abraded skin. By day 14, only 2 animals had this condition.
2. Gross Pathology: As stated above, dry and flaky areas were observed in 2 animals.
3. Histopathology: Hyperkeratosis was observed in the treated skins of 2 animals. This was considered by the Pathologist to be related to treatment and is indicative of mild dermal irritation.
4. Quality Assurance Measures: Signed Good Laboratory Practice Statement and Quality Assurance Statements were provided.

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- C. DISCUSSION: The primary dermal irritation score was 0.3, the test material is considered to be minimally irritating, the study is Core Guideline and the toxicity category is IV.

Reviewed By: Pamela Hurley, Ph.D. *P. Hurley 11/8/89*  
Section I, Tox. Branch, IRS (H7509C)  
Secondary Reviewer: Roger L. Gardner *Roger Gardner*  
Section I, Tox. Branch, IRS (H7509C)

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

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.

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 <sup>a</sup>	Mean Score <sup>b</sup> After Initial Treatment		Mean Score <sup>b</sup> After Challenge		
		24 hr.	48 hr.	24 hr.	48 hr.	72 hr.
Chlorpropham Technical High Dose <sup>c</sup>	0/15	0.3	0.2	0.6	0.1	0.1
Chlorpropham Technical Low Dose <sup>d</sup>	0/15	0.0	0.1	0.8	0.4	0.3
Chlorpropham Technical Irritation Control <sup>e</sup>	---	0.0	0.1	1.7	1.0	0.7
DNCB Positive Control <sup>f</sup>	10/10	0.2	0.8	3.8	3.4	2.9
DNCB Irritation Control <sup>g</sup>	---	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% Chlorpropham Technical w/w in acetone.  
 f) Induced 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

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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