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

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*Approved
for re-
registration
Linnea*

JUL 8 1991

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: ID# 018301. Chlorpropham, technical. Evaluation of Five Acute Toxicity Studies submitted by Chlorpropham Task Force to support reregistration of Chlorpropham.

Shaughnessey No.: 018301
Tox Chem. No.: 510A
Project No.: 1-0640
Submission No.: S390681

TO: Lois Rossi, Team Manager, PM Team 74
Karen Farmer, PM 74 Team Reviewer
Special Review and Reregistration Division (H7508W)

FROM: Linnea J. Hansen, Ph.D.
Section IV, Tox. Branch I (H7509C)
Health Effects Division

Linnea J. Hansen

THRU: Marion P. Copley, D.V.M., D.A.B.T., Section Head
Section IV, Tox. Branch I (H7509C)
Health Effects Division

Marion Copley 6/26/91

CONCLUSIONS:

The acute toxicity studies submitted by the Chlorpropham Task Force for reregistration of Chlorpropham satisfy the guideline requirements and are classified as Acceptable for regulatory purposes. Results of the studies are summarized below:

Acute Oral Toxicity (81-1), Rat	LD ₅₀ = 4.2 kg (both sexes) Toxicity Category III
Acute Dermal Toxicity* (81-2), Rabbit	LD ₅₀ > 2000 mg/kg (both sexes) Toxicity Category III
Primary Ocular Irritation (81-4), Rabbit	Mild irritation, resolved by 72 hr. Toxicity Category III
Primary Dermal Irritation (81-5), Rabbit	PIS 0.1 at 24 and 48 hr (mild irritation. Toxicity Category IV

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Dermal Sensitization
Potential (81-6), G. pig

Not a sensitizer

* Study classified as acceptable despite deficiencies because results are supported by previously submitted acceptable study (MRID# 410137-01)

ACTION REQUESTED:

The Chlorpropham Task Force submitted five acute toxicity studies on April 2 and May 2, 1990 for review to support reregistration of Chlorpropham (CIPC). An acute oral toxicity (81-1), dermal toxicity (81-2), ocular toxicity (81-4), dermal irritation (81-5) and dermal sensitization study (81-6) were submitted. An acute inhalation study (81-3) is not required for reregistration of this compound.

HANSEN/PC-1/CIPC.MEM/0001\CHLORPROPHAM/PROJ 1-0640/ACUTES/6/25/91

2 52

Reviewed by: Linnea J. Hansen, Ph.D. *Linnea J. Hansen 2/21/91*
 Section II, Tox. Branch I (H7509C)
 Secondary reviewer: Marion P. Copley, D.V.M. D.A.B.T.
 Section II, Tox. Branch I (H7509C) *Marion Copley 2/21/91*

DATA EVALUATION REPORT

STUDY TYPE: Primary Ocular Irritation (81-4) TOX. CHEM NO:510A
MRID NO.: 417633-01 SHAUGHNESSEY NO:018301
TEST MATERIAL: Chlorpropham, technical
SYNONYMS: Chlorpropham, technical, 97.1% isopropyl N-(3-chlorophenyl) carbamate. isopropyl N-(3-chlorophenyl) carbanilate, CIPC, Chloro-IPC
STUDY NUMBER: 393E-303-912-89
SPONSOR: Chlorpropham Task Force, c/o John Wise and Associates, Ltd., P.O. Box 336, Liberty, MO 64068.
TESTING FACILITY: T.P.S., Inc., 10424 Middle Mt. Vernon Rd., Mt. Vernon, IN 47620
TITLE OF REPORT: Primary Ocular Irritation Evaluation of Chlorpropham in Rabbits
AUTHOR(S): R.W. Krohmer, Ph.D.
REPORT ISSUED: February 20, 1990

CONCLUSION:

Mild irritation, resolved by 72 hr

<u>HOUR</u>	1	24	48	72
<u>IRRITATION SCORE</u>	6	2.7	0.8	0.0

Toxicity Category: III

Core Classification: Acceptable

This study satisfied the guidelines for Ocular Irritation Studies (Guideline #81-4) and is acceptable for regulatory purposes.

MATERIALS:

- Test compound: Chlorpropham, technical, Description: White crystalline solid, Lot # 14065 L 89, Purity: 97 ± 0.2 % (refer to Study # 393A-101-010-89, Project #1-0640.

2. Test animals: Species: Rabbit, Strain: New Zealand White, Age: young adult, Weight: 3.19-3.52 kg, Source: LSR Industries, Inc., Union Grove, WI.
3. Environment: Rabbits were housed individually in suspended metal cages over flush pans in an isolated room. Temperature: 67-76°F. Humidity: mean 50%. Filtered air was changed 10-15 times/hr. Light: 12 hr light/ 12 hr dark. Food: Purina Complete Rabbit Chow. Water: Tap.

METHODS:

Crystalline Chlorpropham was ground into fine powder and 100 mg placed into the conjunctival sac of one eye per rabbit (3 male and 3 female). The untreated eye acted as control. Animals were restrained until 1 hr after treatment. Eyes were rinsed with saline following the 24 hr evaluation. Ocular examinations were performed prior to treatment and at 1 hr, 24 hr, 48 hr, and 72 hr. Lesions of the cornea, iris, and conjunctivae were noted and graded according to the method of Draize.

Body weight was measured immediately before dosing and at termination (72 hr). Rabbits were examined daily for clinical signs of toxicity.

RESULTS:

TABLE I: PRIMARY OCULAR IRRITATION
AVERAGE SCORES (6 ANIMALS)

OCULAR STRUCTURE	TIME AFTER DOSING (HR)			
	1	24	48	72
Cornea: Opacity	0.0	0.2	0.2	0.0
Area	0.0	0.3	0.2	0.0
Avg. Subtotal (80 max.)	0.0	1.7	0.8	0.0
Iris: Inflammation	0.0	0.0	0.0	0.0
Avg. Subtotal (10 max.)				
Conjunctiva: Redness	1.0	0.2	0.0	0.0
Chemosis	0.0	0.0	0.0	0.0
Discharge	2.0	0.3	0.0	0.0
Avg. Subtotal (20 max.)	6.0	1.0	0.0	0.0
TOTAL AVERAGE SCORES (Max.= 110)	6.0	2.7	0.8	0.0

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Transient conjunctival irritation was observed in all 6 rabbits tested: mild (Score 1) redness and moderate (Score 2) discharge, disappearing by 24 hr in all but one female rabbit. The same animal developed transient, diffuse corneal opacity (Score 1) over 25-50% of the cornea (Score 2). The highest mean irritation score was 6 at 1 hr. Based on these results, Chlorpropham can be assigned to a Toxicity Category of III.

Animals gained or maintained body weight during the study. No clinical signs of systemic toxicity were observed.

Signed Quality Assurance and Good Laboratory Practice Statements were present.

HANSEN/PC-1, CIPC.AOC/0001\Chlorpropham/Proj#1-0640/AcuOcIrrRabbit
5/9/91

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Primary reviewer: David G Anderson, PhD. *David G Anderson 4/30/91*
Section 3, Tox. Branch 1 (H7509C).
Secondary reviewer: Henry Spencer, PhD. *Henry Spencer 5/1/91*
Section 3, Tox. Branch 1 (H7509C).

DATA EVALUATION REPORT

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STUDY TYPE: Acute Oral (81-1)/Rat/Chlorpropham/393A-101-010-89.

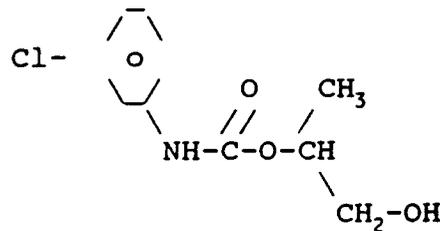
TOX. CHEM. No.: 510A.

MRID No.: 417636-01

TEST MATERIAL: Chlorpropham, technical

SYNONYMS: Chlorpropham, technical, 97.1% isopropyl N-(3-chlorophenyl) carbamate, isopropyl N-(3-chlorophenyl) carbanilate, CIPC, Chloro-IPC.

STRUCTURE:



SPONSOR: Chlorpropham Task Force. & John Wise & Associates, Ltd., P.O. Box 336, Liberty MO, 64068.

TESTING FACILITY: T.P.S., Inc., 10424 Middle Mt. Vernon Road, Mt. Vernon, IN 47620.

STUDY NO.: 393A-101-010-89.

REPORT TITLE: Acute Oral Toxicity Evaluation of Chlorpropham in Rats.

AUTHOR(S): R.W. Krohmer, PhD.

REPORT ISSUED: April 2, 1990.

CONCLUSIONS: Chlorpropham, technical in corn oil was administered in a single dose by gavage to 5 Sprague Dawley rats per sex per dose level at 3000, 4000, 5000 and 6000 mg/kg. Animals dying generally exhibited ataxia and salivation prior to death on day 1 or 2 after dosing.

LD₅₀ for the combined sexes = 4.2 g/kg (95% confidence limits = 3.7-4.8 g/kg). Although the LD₅₀ was combined for males and females, inspection of Table A and B indicates that chlorpropham is Toxicity category III in each sex.

Core classification: Minimum. *(acceptable for regulatory purposes)*

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A. MATERIALS:

1. Test compound: Chlorpropham, technical. Description, white crystalline solid, Batch # 14065L, Purity 97.1%.
2. Test animals: Species: Rat, Strain: Sprague Dawley (CD), Age: ? wk, Weight: Males 151-238 g, Females 132-176 g, Source: Charles River, Inc., Portage MI. Acclimatized ? days.
3. Environment: Rats were housed in wire mesh cages, suspended over flush pans. Temperature: 65-75 °F. Humidity: 50-74%. Filtered air was changed 10-15 times per hour. Light: 12 hr. light/12 hr. dark. Water: Tap. Food: Purina Laboratory Chow # 5001.

B. METHODS:

- Rats were fasted overnight before dosing, and 4-6 hours after.
- Test material was administered orally by gavage in 10 ml of Mazola corn oil/kg body weight.
- Animals were observed continuously for 6 hours after dosing, and twice daily for a total of 14 days.
- Rats were weighed on day 0, 7, and 14, and/or at death.
- Gross necropsy was performed on all animals that died on study and on all survivors which were sacrificed on day 14.
- Doses given and lethality are presented in the Table A under results and discussion.
- The quality assurance statement was signed by D.G. Fehrenbacher, Quality Assurance Auditor, 4/2/90.

C. RESULTS AND DISCUSSION:

Table A.

Test group	Dose in mg/kg	Number animals that died (Day of death)			
		Male	Total	Female	Total
1. ANL2 (LDT)	3000	1(2)	1/5	0	0/5
2. ANL3 (MID1)	4000	1(1), 2(2)	3/5	3(2)	3/5
3. ANL1 (MID2)	5000	2)2)	2/5	1(1), 2(2)	3/5
2. ANL4 (HDT)	6000	2(1), 3(2)	5/5	2(1), 2(2)	4/5

Animals sacrificed at day 14.

Clinical signs were noted in all animals at all dose levels (Table B). Animals receiving 4 g/kg or higher exhibited soiled peritoneal areas in approximately 30% of the animals. Animals dying generally demonstrated ataxia and/or salivation prior to death. Animals demonstrating convulsions died. Animals died on day 1 or 2 after dosing.

Body weight gain was not meaningful because most of the animals died at the higher dose levels and no controls were used.

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Acute Oral (81-1)/Rat/Chlorpropham/393A-101-010-89.

Necropsy indicated that 1 male and 4 females at 5000 mg/kg dose level had clear, yellow or greenish-yellow material in their stomachs. No other lesions were noted.

The LD50 for males and females was 4.2 g/kg with the 95% confidence limits at 3.7 and 4.8 g/kg.

Table B.

Clinical signs exhibited by dosed animals. Some animals demonstrated more than one observation. Zeros mean no entry

Dose group	Observation	15 min		30 min		1 hr		2 hr		3 hr		4 hr		5 hr		6 hr		1 day		2 days		3-14		
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	
3000 mg/kg	Not remarkable	3	2	1	2	0	1	0	2	0	1	0	1	0	0	0	0	0	0	3	3	4	4	5
	Salivation	2	2	2	3	2	3	2	0	2	1	0	1	0	1	0	1	0	0	0	0	0	0	0
	Ataxic	0	0	0	0	2	2	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
	Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
4000 mg/kg	Not remarkable	1	0	2	0	1	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	2
	Salivation	4	5	3	5	3	3	2	2	2	2	2	2	2	3	0	2	0	0	0	0	0	0	0
	Ataxic	0	0	0	0	0	0	0	3	1	4	0	0	0	2	0	0	0	0	0	0	0	0	0
	Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	2	0	0
5000 mg/kg	Not remarkable	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
	Salivation	3	5	3	5	3	5	3	5	3	1	1	0	1	1	1	0	0	0	0	0	0	0	0
	Ataxic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	2	0	0
6000 mg/kg	Not remarkable	1	2	0	2	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0
	Salivation	4	1	4	3	4	2	4	0	4	0	4	0	4	0	2	0	2	0	0	0	0	0	0
	Ataxic	0	0	0	0	1	4	1	2	2	2	1	2	1	1	1	0	1	0	0	0	0	0	0
	Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	3	2	0

Animals with convulsions were not indicated by the tester.

Acute oral/rat/Chlorpropham Task Force/A:\CHLORV25.10A\
DACORRAT.CHL/DANDERSON/4/30/91.*

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Reviewed by: Linnea J. Hansen, Ph.D.
Section VI, Tox. Branch I (~~US-769C~~) H-7509C *Linnea J. Hansen 5/24/90*
Secondary reviewer: Marion P. Copley, D.V.M., D.A.B.T.
Section VI, Tox. Branch I (~~US-769C~~) *Marion Copley 5/24/90*
H-7507C

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal Toxicity (81-2) TOX. CHEM NO: 510A

MRID NO.: 417632-01 SHAUGHNESSEY NO: 018301

TEST MATERIAL: Chlorpropham, technical

SYNONYMS: Chlorpropham, technical, 97.1% isopropyl N-(3-chlorophenyl) carbamate; isopropyl N-(3-chlorophenyl) carbanilate, CIPC, Chloro-IPC.

STUDY NUMBER: 393C-301-210-89

SPONSOR: Chlorpropham Task Force. c/o John Wise & Associates, Ltd., P.O. Box 336, Liberty, MO 64068

TESTING FACILITY: T.P.S., Inc., 10424 Middle Mt. Vernon Rd., Mt. Vernon, IN 47620

TITLE OF REPORT: Acute Dermal Toxicity Evaluation of Chlorpropham in Rabbits

AUTHOR(S): R.W. Krohmer, Ph.D.

REPORT ISSUED: February 28, 1990

CONCLUSION:

Toxicity Category: III

Core Classification: Acceptable

LD₅₀: >2000 mg/kg (Limit Test)

This study alone did not satisfy guidelines for acute dermal toxicity (Guideline #81-2); however, considered together with the data from MRID #410137-04, will be considered acceptable for regulatory purposes.

MATERIALS:

- Test compound: Chlorpropham, technical. Description: White crystalline solid, Batch #: Lot 14065 L 89, Purity - 97.1 ± 0.2% (refer to Study #393A-101-010-89, Project #1-0640).
- Test animals: Species: Rabbit, Strain: New Zealand White, Age: Young adult, Weight: 2.35-2.67 kg (male), 2.31-2.72 kg

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(female),
Source: LSR Industries, Inc., Union Grove, WI.

3. Environment: Rabbits were housed in individual metal cages suspended over flush pans. Temperature: 64-72 64-72° F. Humidity: 45-60%. Filtered air was changed 10-15 times/hr. Light: 12 hr light/ 12 hr dark. Food: Purina Complete Rabbit Chow. Water: Tap.

METHODS:

Five male and 5 female rabbits were shaved 24 hr prior to treatment to give an exposed area of 10% of total body surface. Chlorpropham in melted liquid form was applied to the treatment area (2 g/kg animal body weight). The area was covered with gauze and secured under an occlusive wrap. Rabbits were exposed 24 hr to Chlorpropham. The amount of unabsorbed test material was visually estimated and the area was gently washed with water to remove remaining material. Animals were transferred to clean cages.

Skin reactions were evaluated by the method of Draize 30 min after unwrapping and then twice daily for 14 days. Clinical signs of toxicity were also noted at these times. Body weights were recorded immediately prior to dosing, at 7 days, and at termination (14 days).

Rabbits were sacrificed by carbon dioxide euthanasia and gross necropsies performed.

RESULTS AND DISCUSSION:

No mortality occurred during this study and no significant body weight loss was observed. Clinical signs of toxicity were examined for according to the Methods, but were not mentioned specifically in the Results.

The authors mention that disruption of the coban wrap occurred on 4 animals and loss of the gauze in 2 animals (total 5 animals with disturbed treatment sites). There is no mention of how long after treatment this occurred, but the authors felt that very little test material was lost. This is a subjective judgement, however, and the experiment should have been repeated to guarantee full dosage levels. The authors also use a visual estimation of unabsorbed test material upon removal of the patches, presumably to demonstrate that the wrapped and disturbed animals gave similar results. This estimation is not meaningful and should not be included in future acute dermal toxicity studies.

Sixty percent of the rabbits (3 males and 3 females) developed mild erythema (Score 1) by 30 min after unwrapping. All erythema disappeared by 24 hr and no edema was observed at any time.

LD₅₀: >2 g/kg as determined by limit test

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Gross necropsy showed no remarkable tissue or organ changes. Treated skin surface also did not show remarkable changes.

There are experimental deficiencies in this study but for the following reasons it will be considered acceptable: 1) the results from the animals with disturbed and undisturbed treatment sites are the same and no prolonged irritation was observed; 2) previous acute dermal toxicity studies submitted for the registration of Chlorpropham (MRID 410137-04, core guideline) support the results obtained in this study.

Signed Quality Assurance and Good Laboratory Practice Statements were present.

HANSEN/PC-2, CIPC.ADT/0001\Chlorpropham/Proj#1-0640/AcDermToxRabbit
5/9/91

11 (8)

Reviewed by: Linnea J. Hansen, Ph. D.
Section II, Tox. Branch I (H7509C)
Secondary reviewer: Marion P. Copley, D.V.M., D.A.B.T.
Section II, Tox. Branch I (H7509C)

Linnea J. Hansen 6-25-91

Marion P. Copley
6-26-91

DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation (81-5) TOX. CHEM NO: 510A

MRID NO.: 417635-01 SHAUGHNESSEY NO: 018301

TEST MATERIAL: Chlorpropham, technical

SYNONYMS: Chlorpropham, technical; 97.1% isopropyl N-(3-chlorophenyl) carbamate; isopropyl N-(3-chlorophenyl) carbanilate; CIPC; Chloro-IPC

STUDY NUMBER: 393D-302-211-89

SPONSOR: Chlorpropham Task Force, c/o John Wise and Associates, Ltd., P.O. Box 336, Liberty, MO 64068

TESTING FACILITY: T.P.S., Inc., 10424 Middle Mt. Vernon Rd., Mt. Vernon, IN 47620.

TITLE OF REPORT: Primary Dermal Irritation Evaluation of Chlorpropham in Rats.

AUTHOR(S): R.W. Krohmer, Ph.D.

REPORT ISSUED: February 8, 1990

CONCLUSION:

PIS 0.1 at 24 and 48 hr (mildly irritating)

Toxicity Category: IV

Core Classification: Acceptable

This study satisfied the guidelines for Primary Dermal Irritation (Guideline # 81-5) and is acceptable for regulatory purposes.

MATERIALS:

- Test compound: Chlorpropham, Description: white crystalline solid, Lot No.: 14065 L89, Purity: 97.1% \pm 0.2% (refer to Study No. 393A-101-010-89, Project No.1-0640).
- Test animals: Species: Rabbit, Strain: New Zealand White Albino, Age: Young Adult, Weight: 3.27-3.95 kg,

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Source: LSR Industries, Inc., Union Grove, WI.

3. Environment: Rabbits were housed in individual metal cages suspended over flush pans. Temperature: 70-76° F. Humidity: mean 48%. Filtered air was changed 10-15 times/hr. Light: 12 hr on/12 hr off. Food: Purina Complete Rabbit Chow. Water: Tap.

METHODS:

Crystalline Chlorpropham was melted, cooled and applied in liquid form (0.5 ml/animal) to the shaved, intact skin on the backs of 3 male and 3 female rabbits on an area approximately 6 cm². Application sites were maintained under an occlusive wrap during treatment. After 4 hr treatment, application sites were carefully wiped with water and skin reactions graded at 45 min, 24 hr, 48 hr and 72 hr according to the Draize method. Animal body weights were taken immediately prior to treatment and at 72 hr and animals were monitored for clinical signs of toxicity.

RESULTS AND DISCUSSION:

No edema was observed in any test animal. Very slight erythema (Score 1) was observed in one female rabbit at 24 hr only. A Primary Irritation Index of 0.1 was calculated based on 24 hr and 48 hr scores. Chlorpropham can be classified in Toxicity Category IV for dermal irritation.

All animals survived and gained body weight during the study. No adverse clinical signs were noted.

Experimental deficiencies that should be noted are: 1) the author does not say whether they waited at least 24 hr after shaving to apply test substance; 2) there is no mention of individual observation for the entire day of dosing. These deficiencies do not alter the conclusions drawn from the experiments but should nonetheless be corrected in future studies.

Signed Quality Assurance and Good Laboratory Practice statements were present.

HANSEN/PC-1,CIPC.PDI/0001\Chlorpropham/proj#1-0640/DermIrrRab
5/9/91

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Reviewed by: Linnea J. Hansen, Ph.D. *Linnea J. Hansen* 0-25 91
Section II, Tox. Branch I (H7509C)
Secondary reviewer: Marion P. Copley, D.V.M. D.A.B.T.
Section II, Tox. Branch I (H7509C) *Marion P. Copley 4/26/91*

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization Potential (81-6) TOX. CHEM NO: 510A

MRID NO.: 417634-01 SHAUGHNESSEY NO: 018301

TEST MATERIAL: Chlorpropham, technical

SYNONYMS: Chlorpropham, technical, 97.1% isopropyl N-(3-chlorophenyl) carbamate. isopropyl N-(3-chlorophenyl) carbanilate, CIPC, Chloro-IPC

STUDY NUMBER: 393B-201-215-89

SPONSOR: Chlorpropham Task Force, c/o John Wise and Associates, Ltd., P.O. Box 336, Liberty, MO 64068.

TESTING FACILITY: T.P.S., Inc., 10424 Middle Mt. Vernon Rd., Mt. Vernon, IN 47620

TITLE OF REPORT: Evaluation of the Dermal Sensitization Potential of Chlorpropham in Guinea Pigs

AUTHOR(S): R.W. Krohmer, Ph.D.

REPORT ISSUED: April 6, 1990

CONCLUSION:

Not a sensitizer

Core Classification: Acceptable

This study satisfied the study guidelines for Dermal Sensitization (Guideline #81-6) and is acceptable for regulatory purposes.

MATERIALS:

1. Test compound: Chlorpropham, technical. Description - white crystalline solid, Batch # - Lot 14065 L 89, Purity - 97.1 ± 2.0%.
2. Test animals: Species: Guinea Pig, Female, Strain: Hartley derived American Shorthair albino, Age: young adult, Weight:

366-474 g,

Source: Charles River Laboratories, Inc., Portage, MI.

3. Environment: Guinea pigs were housed in suspended metal cages in an isolated animal room. Temperature: 66-77° F. Humidity: 45-60%. Filtered air was changed 10-15 times/hr. Light: 12 hr light, 12 hr dark. Food: Purina Vitamin C Fortified Guinea Pig Chow. Water: tap.

METHODS:

Guinea pigs were shaved on the left shoulder or flank 24 hr prior to treatment. Each test animal received three inductive applications (0.4g/application at weekly intervals) and one challenge application of ground crystalline Chlorpropham (0.4g /application, 14 days after last inductive dose). Positive controls for dermal sensitization received 3 inductive applications of 0.3% DNCB in 80% ethanol and 1 challenge application of 0.2% DNCB in acetone at the same intervals as the test animals. Test material and DNCB irritation control animals received only the challenge dose. All applications were placed on gauze in a circular plastic chamber except for Test Material Control and Test Material Groups, where gauze was removed to allow space for test material. Chambers were secured underneath taped rubber dams.

Animals were treated for 6 hr and were restrained in stocks during this time. Application chambers were removed and animals were observed daily for response to test material. Animals were depilated and scored for erythema/edema at 24 and 48 hr following the challenge dose according to the method of Draize.

Guinea pigs were weighed immediately prior to initial dose and at weekly intervals thereafter.

RESULTS AND DISCUSSION:

Guinea pigs evaluated 24 and 48 hr after challenge dose showed no sensitization response to Chlorpropham. No erythema or edema was observed at either time. Animals treated only with a challenge dose of Chlorpropham also did not give a response. All guinea pigs in the positive control group showed a sensitization response to DNCB (mean scores 3 for erythema, 1 for edema at 24 hr); those treated only with a challenge dose of DNCB did not respond.

There was no evidence of adverse clinical signs in response to treatments. All but 1 animal gained body weight during the study; this animal developed a rectal prolapse during Week 4 of the study and died on Day 30 despite treatment.

The test material in these experiments was apparently applied without moistening or solubilizing and placed in the patch chamber. It would be preferable to moisten it as described in the Guidelines (81-6) to ensure good contact and absorption. However, results from previous dermal sensitization studies done for registration of

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Chlorpropham (MRID# 410137-07, core guideline) support the results of this study.

Signed Quality Assurance and Good Laboratory Practice Statements were present.

HANSEN/PC-1, CPIC.DSP/0001\CHLORPROPHAM/PROJ#1-0640/DERMESENSGUINPIG
5/9/91