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Chemical Category CHLOROPHENACYLE		

8(e)

3685

CAP

(COMPLIANCE AUDIT PROGRAM)

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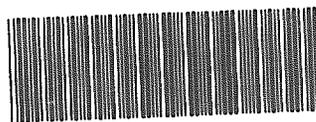
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May 4, 1992

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Washington, DC 20460



88920002327

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes acute toxicity studies with chlorophenacyle (CASRN 103-80-0(?)).

"Chlorophenacyle: Acute Toxicity and Primary irritancy Studies", Bushy Run Research Center, Project Report 50-63, April 27, 1987.

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

Previous PMN submissions related to this substance are: (None)

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,



William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr

Attachment (3 copies of cover letter, summary, and report)

SUMMARY

Project Report 50-63

Chlorophenacyle

Acute Toxicity and Primary Irritancy Studies

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

SUMMARY

Peroral, Rat (Fasted)

Males: LD50 = 0.35 g/kg; sample dosed as a 10% (w/v) suspension in corn oil.

Females: LD50 = 0.23 g/kg; sample dosed as a 10% (w/v) suspension in corn oil.

Percutaneous, Rabbit

Males: 8.0 g/kg killed 0 of 3; sample moistened with distilled water.

Females: 8.0 g/kg killed 0 of 3; sample moistened with distilled water.

Inhalation, Rat; Substantially Saturated Vapor (Static)

Males: 6.0 hours killed 0 of 5.

Females: 6.0 hours killed 0 of 5.

Skin Irritation, Rabbit (4-hr occluded)

Moderate to severe erythema, severe edema, necrosis, desquamation and scabs on 6 of 6 rabbits from 0.5 g (moistened with distilled water).

Corrosive by D.O.T. definition.

Eye Irritation, Rabbit

Severe corneal injury (with vascularization and bulges), severe conjunctival irritation (with necrosis) in one eye from 70 mg (equivalent to 0.1 ml); severe effects through 21 days. Severe corneal injury, iritis, severe conjunctival irritation in 6 eyes from 10 mg (pinpoint pupils also observed in 2); animals sacrificed at 3 days for humane reasons.



BUSHY RUN RESEARCH CENTER

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Telephone (412) 733-5200

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Project Report 50-63
14 Pages
April 27, 1987

Chlorophenacyle

Acute Toxicity and Primary Irritancy Studies

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

SUMMARY

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INTERPRETATION

Chlorophenacyle was highly toxic following its administration by single peroral intubation. It was slightly toxic following single dermal application. A single static inhalation exposure to substantially saturated vapor produced no deaths or other signs of inhalation toxicity. A 4-hour application to covered rabbit skin resulted in severe irritation. Instillation of as little as 10 mg of sample into rabbit eyes produced severe, persistent injury.

SAMPLES

Quantity: 400 g; 400 g (2 samples received)	Submitted By: V. Pinjala
Date Received: January 7, 1987 February 13, 1987	Division: Specialty Chemicals Bound Brook, NJ
Identification: X19149-178; none	UCC Charge No.: 49650
Description: Off-white chunky solid	BRRC Sample No.: 50-3; 50-70
CAS No.: 6305-04-0	BRRC Project No.: 87-15-10819

Additional sample information appears in the attached standard study request form (Appendix 1). Approximately 20 ml of the remaining sample will be retained for 2 years following issuance of this report.

PROCEDURES

Descriptions of the test procedures are included in the attached standard test procedures section (Appendix 2). The sample was ground to a fine powder (using an analytical mill) before dosing. The powder was suspended in corn oil for the peroral dosing. Dermal tests were conducted with the sample moistened with distilled water. For inhalation and eye studies, the dry sample was used.

Dermal toxicity testing was limited to fewer animals than usually dosed because of the difficulties encountered in sample handling. Severe irritation of the eyes, nose and throat among personnel handling the sample was noted when particle respirators were removed following the dosing and wrapping procedures. This material is apparently a strong sensory irritant, and dosing was suspended (with sponsor approval) after sufficient data were collected to assess dermal toxicity. Only one eye was dosed with the "full" amount of sample (70 mg) because of the anticipated severity of ocular response.

RESULTS

Results of the peroral, percutaneous, inhalation and skin irritation tests are given in Tables 1 through 4, respectively. Eye test results are presented in Tables 5 and 6 with a summary appearing in Table 7.

The LD50 for male rats receiving peroral doses of chlorophenacyle was 0.35 g/kg; that for females was 0.23 g/kg. Signs of toxicity included sluggishness, lacrimation, kyphosis, diarrhea, wetness of periurogenital fur, red crust on perinasal and periocular fur and a moribund appearance (in one). Most deaths occurred at 2 hours to 3 days. One female died at 7 days. Survivors recovered at 2 to 4 days. At necropsy, there were pink to red lungs, tan or red stomachs, liquid filled stomachs (filled with white or yellow mucous-like material), a tan pancreas (in one) and clear or red liquid in the thoracic cavity (of 2).

By the percutaneous route, the LD50 for male and female rabbits was greater than 3.0 g/kg. There were no deaths from this (or lower) dosage. One male receiving 16.0 g/kg died after one day. Local dermal effects included erythema, edema, ecchymosis, necrosis, desquamation, fissuring, ulceration and scabs. Except for the one death, there were no signs of systemic toxicity observed. Gross pathologic findings included a few red or mottled lungs, red tracheas (in 2) and one discolored liver.

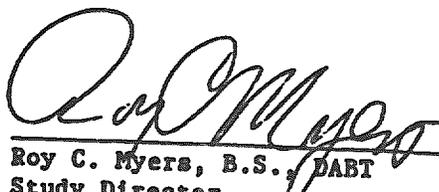
Exposure to a statically-generated, substantially saturated vapor produced no deaths of male or female rats during or following the 6-hour test. There were no signs of toxicity observed. No unusual gross pathology was evident at necropsy.

A 4-hour application of 0.5 g of chlorophenacyle (moistened with distilled water) to occluded rabbit skin resulted in moderate to severe erythema, severe edema and necrosis on 6 of 6 rabbits. Within 7 days, desquamation was observed on 3 rabbits. Erythema and edema became less severe, but necrosis remained on each animal. By 14 days, there was no erythema or edema observed on any rabbit. Scabs or desquamation were apparent on all animals and necrosis persisted on 2. This material is classified as "corrosive" by Department of Transportation (D.O.T.) standards.

Instillation of 70 mg of sample (equivalent to 0.1 ml) into one rabbit eye resulted in severe corneal injury (opacity). Severe conjunctival irritation, with necrosis, also developed in the rabbit. The iris was not visible because of the severe corneal opacity and conjunctival swelling. After 7 days, there was a red, pus-like ocular discharge. By 14 days, the eye developed corneal vascularization. Severe injury, with an irregular corneal shape (characterized by surface bulges), persisted through 21 days.

After instillation of 10 mg, 6 of 6 eyes developed severe corneal opacity. There was iritis in most rabbits, although examination of the iris was difficult or impossible because of corneal opacity and conjunctival swelling. Severe conjunctival irritation appeared in all 6 eyes. At the one hour reading, 2 rabbits exhibited pin-point pupils. This effect did not persist at 4 hours. There was a pus-like ocular discharge in all eyes at 2 days. One also had conjunctival necrosis. Severe injury persisted at 3 days and, with sponsor authorization, all 6 rabbits were sacrificed.

Reviewed and Approved by:


Roy C. Myers, B.S., DABT
Study Director
4-27-87
Date


Ronald S. Slesinski, Ph.D., DABT
Assistant Director
4-27-87
Date


Fred R. Frank, Ph.D.
Director
4/27/87
Date

Acknowledgements:

Single Peroral Tests

Percutaneous, Skin and Eye
Irritation Tests

Inhalation Studies

Todd A. Christopher, AALAS II
Associate Technician

Kathleen R. Hufford, AALAS Cert. II
Technologist

Nick S. Bellich, AALAS Cert. II
Master Technologist

Larry E. Lipko, AALAS II
Associate Technician

WPC/kam/0807K-2
04/15/87

Table 2

Dermal Application, Single Dose to Rabbits

Sample No.: 50-3; 50-70

Material: Chlorophenacyle

Dosage, Dead/ Days to Mean Weight, R. ± S.D.
 g/kg. Dosed* Death 0 Days 7 Days 14 Days 21 Days 28 Days Skin Irritation Signs of Toxicity Gross Pathology

Male Rabbits

Dosage g/kg.	Dead/ Days to Death	0 Days	7 Days	14 Days	21 Days	28 Days	Skin Irritation	Signs of Toxicity	Gross Pathology
16.0	1/1	1	2344	-	-	-	Erythema, edema, necrosis.	None noted before death.	Trachea red; liver discolored.
8.0	0/3	-	2610± 280	2539± 216	2807± 298	-	Erythema at 1 to 7 days; edema, necrosis at 1 to 14 days; desquamation at 7 to 14 days; scabs, fissuring, ulceration (on 1) at 14 days.	None noted.	Lungs of 1 mottled light and dark red; trachea of 1 red.
4.0	0/1	-	2747	2806	3013	-	Erythema, edema at 1 to 7 days; necrosis at 1 to 14 days; fissuring at 14 days.	None noted.	Nothing remarkable.
2.0	0/1	-	2420	2456	2592	-	Erythema, edema, necrosis at 1 to 14 days; ecchymosis at 1 day; desquamation at 7 to 14 days.	None noted.	Nothing remarkable.

(Continued)

Table 2 (Continued)

Dermal Application, Single Dose to Rabbits

Material: Chlorophenacyle	Mean Weight, $\bar{x} \pm$ S.D.		Sample No.: 50-3: 50-70
	Dosage, Dead/ Days to Death	Dosage, Days to Death	
\bar{x} /kg	0 Days	7 Days	14 Days
Signs of Toxicity			
Skin Irritation			
Gross Pathology			
8.0	0/3	2584± 81	2723± 196
Female Rabbits			
			Erythema at 1 to 7 days; edema, necrosis at 1 to 14 days; desquamation at 7 to 14 days; fissuring, scabs (on 1), ulceration (on 1) at 14 days.
			None noted.
			Lungs with dark red patches.

LD50s:

Males: 8.0 g/kg killed 0 of 3; sample moistened with distilled water.
Females: 8.0 g/kg killed 0 of 3; sample moistened with distilled water.

*The usual numbers of animals were not included in this study because of severe sensory irritation experienced by personnel handling the test material.

WPG/kam/0807K-1
04/15/87

Table 4

Primary Skin Irritation - Rabbit

Material: Chlorophenacyle Sample No.: 50-3 Conditions: 0.5 g. (moistened with 0.5 ml distilled water)

Date: 02-10-87	Date: 02-10-87	Date: 02-10-87	Date: 02-10-87
Rabbit No: 87-3747	Rabbit No: 87-3748	Rabbit No: 87-3749	Rabbit No: 87-3778
Sex: Male	Sex: Male	Sex: Male	Sex: Female
Date: 02-10-87	Date: 02-10-87	Date: 02-10-87	Date: 02-10-87
Rabbit No: 87-3781	Rabbit No: 87-3782	Rabbit No: 87-3783	Rabbit No: 87-3784
Sex: Female	Sex: Female	Sex: Female	Sex: Female

Erythema & Eschar Formation

Time (After Initiation of Contact):	Score	Mean Score						
5 hours	3	3	3	3	3	3	3	3.0
1 day	4	3	3	2	4	4	4	3.3
2 days	4	3	3	1	4	4	4	3.2
3 days	4	3	3	0	3	4	4	2.8
7 days	2	1	2	0	1	2	2	1.3
10 days	0	1	1	0	0	0	0	0.3
14 days	0	0	0	0	0	0	0	0.0

Edema Formation

Time:	Score	Mean Score						
5 hours	4	4	4	4	4	4	4	4.0
1 day	4	4	1	2	3	4	4	3.0
2 days	3	4	1	0	3	4	4	2.5
3 days	2	2	1	0	2	2	2	1.5
7 days	1	2	1	0	1	2	2	1.2
10 days	1	2	0	0	0	1	1	0.7
14 days	0	0	0	0	0	0	0	0.0

Other Irritation or Effects

Time:	Effect						
5 hours	None						
1 day	N	N	N	N	N	N	N
2 days	N	N	N	N	N	N	N
3 days	N	N	N	N	N	N	N
7 days	N,D	N	N	N	N	N	N
10 days	N,S	N	N	N	N	N	N
14 days	N,S	N,S	N	N	N	N	N,S

Specific Effects/Remarks: D = desquamation; N = necrosis; S = scab formation.

Table 5

Primary Eye Irritation-Rabbit

Material: Chlorophenacyle Sample No.: 50-3 Amount: 70 mg

Rabbit No:	87-5074
Sex/Eye Dosed	Male/R
Date Dosed	02-24-87

			Scores/Effects at 1 hr					Mean
Cornea:	Opacity	*						*
	Area	*						*
Iris:	Inflam.	*						*
	Redness	1						1
Conjunct:	Chemosis	4						4
	Discharge	3						3
Other Effects/Remarks:								

			Scores/Effects at 4 hr					Mean
Cornea:	Opacity	*						*
	Area	*						*
Iris:	Inflam.	*						*
	Redness	3						3
Conjunct:	Chemosis	4						4
	Discharge	3						3
Other Effects/Remarks:								

			Scores/Effects at 24 hr					Mean
Cornea:	Opacity	*						*
	Area	*						*
Iris:	Inflam.	*						*
	Redness	3						3
Conjunct:	Chemosis	4						4
	Discharge	3						3
Fluorescein Exam.	*							*
Other Effects/Remarks: Necrosis of the conjunctivae and nictitating membrane; red discharge.								

			Scores/Effects at 48 hr					Mean
Cornea:	Opacity	*						*
	Area	*						*
Iris:	Inflam.	*						*
	Redness	3						3
Conjunct:	Chemosis	4						4
	Discharge	3						3
Fluorescein Exam.	*							*
Other Effects/Remarks: Necrosis of the conjunctivae and nictitating membrane; red discharge.								

(Continued)

Table 5 (Continued)

Primary Eye Irritation-Rabbit

Material: Chlorophenacyle Sample No.: 50-3 Amount: 70 mg

Rabbit No:	87-5074
Sex/Eye Dosed	Male/R
Date Dosed	02-24-87

		Scores/Effects at 72 hr						Mean
Cornea:	Opacity	4						4
	Area	*						*
Iris:	Inflam.	*						*
	Redness	3						3
Conjunct:	Chemosis	4						4
	Discharge	3						3
	Fluorescein Exam.	*						*
Other Effects/Remarks:		Necrosis of the conjunctivae and nictitating membrane; pus-like, red discharge.						

		Scores/Effects at 7 days						Mean
Cornea:	Opacity	4						4
	Area	*						*
Iris:	Inflam.	*						*
	Redness	2						2
Conjunct:	Chemosis	3						3
	Discharge	3						3
	Fluorescein Exam.	*						*
Other Effects/Remarks:		Necrosis of the conjunctivae and nictitating membrane; pus-like, red discharge.						

		Scores/Effects at 14 days						Mean
Cornea:	Opacity	4						4
	Area	4						4
Iris:	Inflam.	*						*
	Redness	1						1
Conjunct:	Chemosis	3						3
	Discharge	2						2
	Fluorescein Exam.	40%						40%
Other Effects/Remarks:		Corneal vascularization; pus-like discharge.						

		Scores/Effects at 21 days						Mean
Cornea:	Opacity	4						4
	Area	4						4
Iris:	Inflam.	*						*
	Redness	1						1
Conjunct:	Chemosis	2						2
	Discharge	3						3
	Fluorescein Exam.	60%						60%
Other Effects/Remarks:		Corneal vascularization; irregular corneal shape.						

*Scoring not possible because of severe conjunctival swelling and/or corneal opacity.

Table 6

Primary Eye Irritation-Rabbit

Material: Chlorophenacyle Sample No.: 50-3 Amount: 10 mg

Rabbit No:	87-6055	87-6056	87-6057	87-6086	87-6087	87-6088	
Sex/Eye Dosed	Male/R	Male/L	Male/R	Female/L	Female/R	Female/L	
Date Dosed	03-17-87	03-17-87	03-17-87	03-17-87	03-17-87	03-17-87	

Scores/Effects at 1 hr								Mean
Cornea:	Opacity	1	1	*	*	1	1	*
	Area	*	*	*	*	*	*	*
Iris:	Inflam.	1	1	*	*	1	1	*
Conjunct:	Redness	1	1	1	1	1	1	1.0
	Chemosis	4	4	4	4	4	4	4.0
	Discharge	3	3	3	3	3	3	3.0

Other Effects/Remarks: Rabbits 6055 and 6088 with a pin-point pupil.

Scores/Effects at 4 hr								Mean
Cornea:	Opacity	2	1	*	*	1	1	*
	Area	*	*	*	*	*	*	*
Iris:	Inflam.	1	1	*	*	1	1	*
Conjunct:	Redness	3	3	3	3	3	3	3.0
	Chemosis	4	4	4	4	4	4	4.0
	Discharge	3	3	3	3	3	3	3.0

Other Effects/Remarks:

Scores/Effects at 24 hr								Mean
Cornea:	Opacity	4	2	*	*	2	2	*
	Area	*	3	*	*	*	*	*
Iris:	Inflam.	*	1	*	*	*	*	*
Conjunct:	Redness	3	3	3	3	3	3	3.0
	Chemosis	4	3	4	4	4	4	3.8
	Discharge	3	3	3	3	3	3	3.0
Fluorescein Exam.		*	*	*	*	*	*	*

Other Effects/Remarks:

Scores/Effects at 48 hr								Mean
Cornea:	Opacity	4	3	4	4	3	3	3.5
	Area	*	*	*	*	4	*	*
Iris:	Inflam.	*	*	*	*	*	*	*
Conjunct:	Redness	2	2	3	3	2	2	2.3
	Chemosis	3	3	4	4	3	4	3.5
	Discharge	3	3	3	3	3	3	3.0
Fluorescein Exam.		*	*	*	*	60%	*	*

Other Effects/Remarks: All rabbits with a pus-like ocular discharge; Rabbit 6086 with necrosis of the conjunctivae.

Scores/Effects at 72 hr								Mean
Cornea:	Opacity	3	2	4	4	4	3	3.3
	Area	4	4	*	3	4	4	*
Iris:	Inflam.	*	1	*	1	*	*	*
Conjunct:	Redness	1	1	1	1	1	1	1.0
	Chemosis	2	1	4	4	3	3	2.8
	Discharge	2	1	3	3	3	3	2.5
Fluorescein Exam.		20%	5%	*	40%	5%	20%	*

Other Effects/Remarks: Rabbits sacrificed after 72-hour reading for humane reasons.

*Scoring not possible because of severe conjunctival swelling and/or corneal opacity.

Table 7

Summary of Eye Scores

Material: <u>Chlorophenacyle</u>		Sample No: <u>50-3</u>					
OBSERVATION		OBSERVATION TIMES					
		1 Hr	4 Hr	24 Hr	48 Hr	72 Hr	7 Days
		Amount Instilled: 70 mg (one eye dosed)					
CORNEA							
Opacity:	Range	*	*	*	*	4	4
	Mean	-	-	-	-	-	-
Area:	Range	*	*	*	*	*	*
	Mean	-	-	-	-	-	-
IRIS							
Injury:	Range	*	*	*	*	*	*
	Mean	-	-	-	-	-	-
CONJUNCTIVAE							
Redness:	Range	1	3	3	3	3	2
	Mean	-	-	-	-	3	3
Chemosis:	Range	4	4	4	4	4	3
	Mean	-	-	-	-	-	-
Discharge:	Range	3	3	3	3	3	3
	Mean	-	-	-	-	-	-
		Amount Instilled: 10 mg					
CORNEA							
Opacity:	Range	*	*	*	3 to 4	2 to 4	-
	Mean	*	*	*	3.5	3.3	-
Area:	Range	*	*	*	*	*	-
	Mean	*	*	*	*	*	-
IRIS							
Injury:	Range	*	*	*	*	*	-
	Mean	*	*	*	*	*	-
CONJUNCTIVAE							
Redness:	Range	All 1	All 3	All 3	2 to 3	All 1	-
	Mean	1.0	3.0	3.0	2.3	1.0	-
Chemosis:	Range	All 4	All 4	3 to 4	3 to 4	1 to 4	-
	Mean	4.0	4.0	3.8	3.5	2.8	-
Discharge:	Range	All 3	All 3	All 3	All 3	1 to 3	-
	Mean	3.0	3.0	3.0	3.0	2.5	-

* Scoring of cornea and/or iris not possible in some eyes because of severe conjunctival swelling and/or corneal opacity.
 ** Rabbit receiving 70 mg had severe eye injury through 21 days; rabbits dosed with 10 mg were sacrificed after 3 days.