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Chemical Category HEXYL CELLOSOLVE		

8(e)

3663

CAP

(COMPLIANCE AUDIT PROGRAM)

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May 4, 1992

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U.S. Environmental Protection Agency
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88920002325

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

Re: CAP Agreement Identification: 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 hexyl CELLOSOLVE® (CASRN 112-25-4).

"Hexyl CELLOSOLVE®: Acute Toxicity and Primary Irritancy Studies", Bushy Run Research Center, Project Report 49-194, March 6, 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 49-194

Hexyl CELLOSOLVE®

Acute Toxicity and Primary Irritancy Studies

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

* * * * *

SUMMARY

Peroral, Rat (Fasted)

Males: LD50 = 1.67 ml/kg; sample dosed as received.

Females: LD50 = 0.83 ml/kg; sample dosed as received.

Percutaneous, Rabbit

Males: LD50 = 0.81 ml/kg; sample dosed as received.

Females: LD50 = 0.93 ml/kg; sample dosed as received.

Severe irritation observed.

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)

Minor to moderate erythema on 5 of 6 rabbits, moderate edema on 4, desquamation on 4, necrosis on 3 from 0.5 ml.

Corrosive by D.O.T. definition.

Eye Irritation, Rabbit

Minor, diffuse corneal injury in 6 of 6 eyes, iritis in 6, moderate to severe conjunctival irritation in 6 from 0.005 ml; 4 healed at 3 days; all healed at 7 days.



BUSHY RUN RESEARCH CENTER

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Telephone (412) 733-5200

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Project Report 49-194
13 Pages
March 6, 1987

Hexyl CELLOSOLVE®

Acute Toxicity and Primary Irritancy Studies

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

* * * * *

SUMMARY

Peroral, Rat (Fasted)

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Eye Irritation, Rabbit

Minor, diffuse corneal injury in 6 of 6 eyes, iritis in 6, moderate to severe conjunctival irritation in 6 from 0.005 ml; 4 healed at 3 days; all healed at 7 days.

INTERPRETATION

Hexyl CELLOSOLVE® was moderately toxic following its administration by single peroral intubation and 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 0.005 ml of sample into rabbit eyes produced moderate to severe irritation.

SAMPLE

Quantity: 10 gal.	Submitted By: W. F. Gorham
Date Received: April 14, 1986	Division: Specialty Chemicals Bound Brook, NJ (sample from South Charleston, WV)
Identification: Lot S074565	Sponsor Charge No.: None
Description: Clear, non-viscous liquid	BRRC Sample No.: 49-101
CAS No.: 112-25-4	BRRC Project No.: 86-15-10797

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 1). The sample was dosed as received for all tests.

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 Table 5 with a summary appearing in Table 6.

The LD50 for male rats receiving peroral doses of Hexyl CELLOSOLVE® was 1.67 ml/kg; that for females was 0.83 ml/kg. Signs of toxicity included sluggishness, lacrimation, drooping eyelids, piloerection, labored breathing, red perinasal discharge (in 2) and prostration. Deaths occurred at 3 hours to 3 days. Survivors recovered at one to 3 days. At necropsy, there were mottled and red lungs, red or liquid-filled stomachs, urinary bladders with red fluid and one liver nodule.

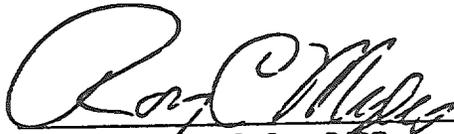
By the percutaneous route, the LD50 for male rabbits was 0.81 ml/kg. The LD50 for females was 0.93 ml/kg. Local dermal effects included erythema, edema, ecchymosis, necrosis, desquamation, scabs and ulceration. A comatose appearance, red perinasal discharge, sluggishness and an unsteady gait were among the signs of toxicity observed. Time to death ranged from one to 3 days. Survivors recovered at 2 to 4 days. Gross pathologic findings included mottled and pink to red lungs, red thymuses, a few red tracheas and dorsal alopecia.

Exposure to a statically-generated, substantially saturated vapor produced no deaths of 5 male or 5 female rats during or following the 6-hour test. There were no signs of toxicity or remarkable gross pathologic lesions observed.

A 4-hour application of 0.5 ml of Hexyl CELLOSOLVE® to occluded rabbit skin resulted in minor to moderate erythema on 5 of 6 rabbits and moderate edema on 4. After one day, necrosis was apparent on 3 females and persisted through 7 days. No erythema or edema remained after 7 days. Four rabbits exhibited desquamation. By Department of Transportation (D.O.T.) definition, this material was corrosive to the skin.

Instillation of 0.005 ml of sample into rabbit eyes resulted in minor, diffuse corneal injury (opacity) in 6 of 6 animals. Iritis was apparent in all 6 eyes and moderate to severe conjunctival irritation developed in all 6 rabbits. After 48 hours, 2 rabbits exhibited complete healing. By 72 hours, 4 eyes had a normal appearance and 2 still had minor corneal effects. All 6 eyes were healed after 7 days.

Reviewed and Approved by:


Roy C. Myers, B.S., DABT 3-6-87
Study Director Date


Ronald S. Slesinski, Ph.D., DABT 3-6-87
Assistant Director Date


Fred R. Frank, Ph.D. 3/6/87
Director Date

Acknowledgements:

Single Peroral Tests

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Eye Irritation Tests

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Technologist

Nick S. Bellich, AALAS Cert. II
Master Technologist

Mary G. Brawley, HT (ASCP)
Master Technologist

Inhalation Studies

David W. Fait, B.S., AALAS Cert II
Master Technologist

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Table 1

Peroral Intubation, Single Dose to Rats

Sample No.: 49-101

Material: Hexyl CELLOSOLVE®

Dosage, ml/kg.	Dead/ Dosed	Days to Death	Mean Weight, $\bar{x} \pm$ S.D.		Signs of Toxicity	Gross Pathology	
			0 Days	7 Days			
2.00	5/5	1,1,1,1,3	210± 5.1	-	Sluggishness, lacrimation at 2 hr; drooping eyelids, prostration at 3.5 hr; moribund appearance at 3.5 hr to 1 day; piloerection, labored breathing at 2 days.	Lungs mottled light and dark red; stomachs of 2 liquid-filled; bladders of 2 liquid-filled.	
1.41	0/5	-	214± 2.0	253± 8.1	284± 21.4	Sluggishness, lacrimation at 1 day; marked sluggishness, kyphosis in 1 at 1 day; red discharge on perinasal fur of 2 at 1 to 2 days. Recovery at 2 to 3 days.	Nothing remarkable.
1.00	0/5	-	212± 9.3	261± 17.4	297± 10.5	Sluggishness at 3 hr. Recovery at 1 day.	Nothing remarkable.
0.50	0/3	-	221± 5.0	284± 12.1	313± 14.2	None noted.	Nothing remarkable.

(Continued)

Table 1 (Continued)

Peroral Intubation, Single Dose to Rats

Material: Hexyl CELLOSOLVE Sample No.: 49-101

Dosage, ml/kg	Dead/ Dosed	Days to Death	Mean Weight, $\bar{x} \pm$ S.D.			Signs of Toxicity	Gross Pathology
			0 Days	7 Days	14 Days		
4.0	3/3	0,1,1	217± 14.8	-	-	Sluggishness, lacrimation, piloerection at 3 hr; unsteady gait, prostration in 1 at 3 hr. Death of 1 at 3 hr.	Lungs dark pink; non-glandular portion of stomach red; urinary bladder with red liquid.
2.0	3/3	1,1,1	215± 7.5	-	-	Sluggishness, lacrimation, prostration, slight piloerection at 3 hr.	Lungs dark pink; non-glandular portion of stomach red; urinary bladder of 1 red.
1.0	5/5	1,1,1,1,2	211± 6.3	-	-	Sluggishness, lacrimation at 2 hr; prostration at 4 hr; moribund appearance in 1 at 4 hr.	Lungs red; stomachs of 2 liquid-filled; intestines red.
0.71	0/5	-	218± 13.9	241± 17.5	248± 20.7	None noted.	Lungs dark red.
0.50	0/5	-	218± 10.1	241± 11.7	248± 12.7	None noted.	Liver of 1 with nodule.
0.25	0/5	-	220± 8.7	236± 12.1	245± 10.9	None noted.	Nothing remarkable.

LD50s with 95% Confidence Limits:
Males: 1.67 (1.43 to 1.96) ml/kg; sample dosed as received.
Females: 0.83 (0.71 to 0.97) ml/kg; sample dosed as a received.

LD50 Slopes:
Males: 13.1
Females: 12.8

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Female Rats

Table 2

Dermal Application, Single Dose to Rabbits

Material: Hexyl CELLOSOLVESample No.: 49-101

Dosage, Dead/ Dosed Days to Death Mean Weight, g \pm S.D. 0 Days 7 Days 14 Days Skin Irritation Signs of Toxicity Gross Pathology

Male Rabbits

4.0	5/5	1,1,1,1,1	2436 \pm 130	-	-	Sample residue, erythema, edema, ecchymosis, necrosis at 1 day (death).	Comatose appearance at 20 min.	Lungs dark pink.
2.0	5/5	1,1,1,1,1	2518 \pm 90	-	-	Sample residue, erythema, edema, ecchymosis, necrosis at 1 day (death).	Comatose appearance at 30 min; red discharge around nose of 2 at 1 day.	Lungs mottled light and dark pink; thymuses light red.
1.0	4/5	1,1,1,2	2663 \pm 186	2517	2817	Sample residue at 1 day; erythema, edema, necrosis at 1 day, persisting on 1 to 14 days; scabs on 1 at 14 days.	Comatose appearance at 30 min; sluggishness, unsteady gait in 2 at 1 day. Survivor recovered at 2 days.	In victims, lungs of 2 pink; thymus of 1 red. In survivor, trachea with red patches.
0.5	0/5	-	2631 \pm 201	2647 \pm 179	2804 \pm 211	Sample residue at 1 day; erythema, edema, necrosis at 1 to 14 days; desquamation, scabs, ulceration at 14 days.	Sluggishness in 2, unsteady gait in 1 at 1 day. Recovery at 4 days.	Lungs of 1 mottled pink to dark red; alopecia of dorsal surface; thoracic cavity of 1 with clear fluid.

(Continued)

Table 3

Inhalation of Substantially Saturated Vapor, Single Exposure to Rats; Static Conditions at 26°C

Material: Hexyl CELLOSOLVE Sample No.: 49-101

Dead/ Days to Mean Weight, $\bar{x} \pm$ S.D. Signs of Toxicity Gross Pathology
 Duration Dosed Death 0 Days 7 Days 14 Days

Male Rats

6.0 hr 0/5 - 220± 250± 271± None noted. Nothing remarkable.
 4.0 3.4 5.1

Female Rats

6.0 hr 0/5 - 234± 234± 236± None noted. Nothing remarkable.
 6.2 3.4 4.3

LT50's:

Males: 6.0 hours of exposure killed 0 of 5.
 Females: 6.0 hours of exposure killed 0 of 5.

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Table 5

Primary Eye Irritation-Rabbit

Material: Hexyl CELLOSOLVE® Sample No.: 49-101 Amount: 0.005 ml

Rabbit No:	86-1968	86-2086	86-2087	86-2121	86-2122	86-2123
Sex/Eye Dosed	Male/R	Male/L	Male/R	Female/L	Female/R	Female/L
Date Dosed	11-18-86	11-18-86	11-18-86	11-18-86	11-18-86	11-18-86

Scores/Effects at 1 hr							Mean
Cornea:	Opacity	1	1	1	1	1	1.0
	Area	3	3	2	3	2	2.5
Iris:	Inflam.	1	1	1	1	1	1.0
Conjunct:	Redness	1	1	1	1	1	1.0
	Chemosis	3	4	3	2	3	3.0
	Discharge	3	3	3	2	3	2.8

Other Effects/Remarks:

Scores/Effects at 4 hr							Mean
Cornea:	Opacity	1	1	1	1	1	1.0
	Area	2	3	3	3	2	2.5
Iris:	Inflam.	1	1	1	1	1	1.0
Conjunct:	Redness	1	1	1	1	1	1.0
	Chemosis	3	3	4	3	3	3.2
	Discharge	3	3	3	2	3	2.8

Other Effects/Remarks: Rabbit 2087 with a pus-like ocular discharge.

Scores/Effects at 24 hr							Mean
Cornea:	Opacity	0	1	1	1	1	0.8
	Area	0	3	2	2	1	1.7
Iris:	Inflam.	0	1	1	1	0	0.7
Conjunct:	Redness	1	1	1	1	1	1.0
	Chemosis	0	2	2	1	1	1.2
	Discharge	1	2	1	1	1	1.2
Fluorescein Exam.		20%	70%	70%	60%	50%	47%

Other Effects/Remarks: Rabbit 2086 with a pus-like ocular discharge.

Scores/Effects at 48 hr							Mean
Cornea:	Opacity	0	1	1	1	0	0.5
	Area	0	4	3	1	0	1.3
Iris:	Inflam.	0	1	1	1	0	0.5
Conjunct:	Redness	0	1	1	1	0	0.5
	Chemosis	0	1	0	0	0	0.2
	Discharge	0	1	0	0	0	0.2
Fluorescein Exam.		0%	40%	50%	20%	30%	23%

Other Effects/Remarks:

Scores/Effects at 72 hr							Mean
Cornea:	Opacity	0	1	1	0	0	0.3
	Area	0	3	3	0	0	1.0
Iris:	Inflam.	0	0	0	0	0	0.0
Conjunct:	Redness	0	0	0	0	0	0.0
	Chemosis	0	0	0	0	0	0.0
	Discharge	0	0	0	0	0	0.0
Fluorescein Exam.		0%	15%	35%	0%	0%	8%

Other Effects/Remarks:

(Continued)

Table 5 (Continued)

Primary Eye Irritation-Rabbit

Material: Hexyl CELLOSOLVE® Sample No.: 49-101 Amount: 0.005 ml

Rabbit No:	86-1968	86-2086	86-2087	86-2121	86-2122	86-2123	
Sex/Eye Dosed	Male/R	Male/L	Male/R	Female/L	Female/R	Female/L	
Date Dosed	11-18-86	11-18-86	11-18-86	11-18-86	11-18-86	11-18-86	
Scores/Effects at 7 days							
Cornea: Opacity	0	0	0	0	0	0	Mea
Area	0	0	0	0	0	0	0.
Iris: Inflamm.	0	0	0	0	0	0	0.
Conjunct: Redness	0	0	0	0	0	0	0.
Chemosis	0	0	0	0	0	0	0.
Discharge	0	0	0	0	0	0	0.
Fluorescein Exam.	0%	0%	0%	0%	0%	0%	0.
Other Effects/Remarks:							0%

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Table 6

Summary of Eye ScoresMaterial: Hexyl CELLOSOLVE®Sample No: 49-101

OBSERVATION	OBSERVATION TIMES						
	1 Hr	4 Hr	24 Hr	48 Hr	72 Hr	7 Days	
Volume Instilled: 0.005 ml							
CORNEA							
Opacity:	Range	All 1	All 1	0 to 1	0 to 1	0 to 1	All 0
	Mean	1.0	1.0	0.8	0.5	0.3	0.0
Area:	Range	2 to 3	2 to 3	0 to 3	0 to 4	0 to 3	All 0
	Mean	2.5	2.5	1.7	1.3	1.0	0.0
IRIS							
Injury:	Range	All 1	All 1	0 to 1	0 to 1	All 0	All 0
	Mean	1.0	1.0	0.7	0.5	0.0	0.0
CONJUNCTIVAE							
Redness:	Range	All 1	All 1	All 1	0 to 1	All 0	All 0
	Mean	1.0	1.0	1.0	0.5	0.0	0.0
Chemosis:	Range	2 to 4	3 to 4	0 to 2	0 to 1	All 0	All 0
	Mean	3.0	3.2	1.2	0.2	0.0	0.0
Discharge:	Range	2 to 3	2 to 3	1 to 2	0 to 1	All 0	All 0
	Mean	2.8	2.8	1.2	0.2	0.0	0.0

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