



UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

September 22, 1992

A

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Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

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 an acute toxicity study with CELLOSOLVE® (ethylene glycol monoethyl ether; CASRN 110-80-5).

"The Subacute Toxicity of "Cellosolve"", Mellon Institute of Industrial Research (University of Pittsburgh), Report 10-93, 9/3/47.

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)

12/1/94

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)

3

SUMMARY

Confidential

R: 9-3-47

Report 10-93

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

The Subacute Toxicity of "Cellosolve"

Tables of Protocols Attached

Carbide and Carbon Chemicals Corporation Industrial Fellowship No. 274-10

Summary

"Cellosolve" was fed to rats in their drinking water for 90 days at intake levels of 1.888, 0.735, 0.213, 0.052, and 0.0 gm./kg./day. The highest level produced 100% mortality at the end of 38 doses and the next highest level produced significant effects on appetite, growth, and organ weight. Male rats that succumbed to both of these concentrations showed micropathological testicular damage and the rats that received 1.888 gm./kg./day showed cloudy swelling of the kidney and liver. The dosage level of 0.213 gm./kg./day showed no effect. In accordance with Report 10-84 on Subacute Doses one would say that "Cellosolve" shows some subacute action as the degree of chronic activity is higher than would be expected from the acute toxicity of the material. "Cellosolve" is similar to "Carbitol" CBM and GF in subacute oral toxicity.

Number copies made 6
Number copies mailed 2 by MEI
Date of mailing 9-9-47
I-A.C. CRANCH
Addressed to I-A.C. KAMMER

testicular effects

B-11

Confidential

Report 10-93

230-2-54

B(a) 29
R: 9-3-47

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

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The Subacute Toxicity of "Cellosolve"

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Previous Work and Literature

In late 1946 after we believed we had uncovered the reason for our troubles with rat lung infections we desired to check our findings by running a 90-day oral dose study with particularly careful observation of the rats. It did not seem wise to study a material of pressing current interest because we were not certain that the work could be carried through satisfactorily. Therefore older materials for which comparative data were desired were selected. The choice fell on "Cellosolve" and methyl "Cellosolve". A combination of accidents vitiated the results upon the latter.

The acute oral toxicity to rats and guinea pigs of "Cellosolve" was indicated in a report dated 5-20-38. The LD₅₀'s were 3.00 (2.51 to 3.59) and 1.40 (1.22 to 1.60) respectively. Morris, Nelson and Calvery (1) reported testicular damage in two-thirds of their male rats as a result of two years of dosage to 2.16% "Cellosolve" in the diet as well as slight chronic kidney damage and no chronic liver damage. They also reported few damaged testes, no chronic kidney and slight chronic liver injury in the rats that received two years of dosage to "Carbitol" while we indicated only one case of testicular damage and chronic liver and kidney injury in our report 7-31, dated 4-17-47.

Sample

One gallon of commercial grade "Cellosolve" was furnished by Fellowship 155 on 12-11-46. No analytical details accompanied the sample.

B-11

testicular effects

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I.A.C. CRANW
Addressed to I.A.C. KAMMER

Subacute Doses

During a period of 90 days, doses of "Cellosolve" were administered to 4 to 8 male and 4 to 8 female Sprague-Dawley strain rats at known concentrations in the drinking water. The animals received Purina Laboratory Chow Meal as their dry diet. The control rats received identical treatment as did the experimental except that no "Cellosolve" was placed in their drinking water.

Table 10-249 summarizes the results.

Table 10-249

Results of 90-day Doses in the Drinking Water

Dosage in gm./kg./day	1.888	0.735	0.213	0.052	0.000
Concentration in the drinking water, %	2.56	0.64	0.16	0.04	0.00
Ml. water drunk/rat/day	8.168*	19.294*	25.391	26,029	26.789
Gms. diet eaten/rat/day	4.080*	11.079*	13.057	14,009	14.513
Mean weight gain of surviving rats	-	+80.0*	+113.1	+109.5	+138.3
Mean body length in m.m. at sacrifice	-	203.8*	213.6	220.2	218.2
Fatness (gms. per m.m. body length)	-	0.976*	1.096	1.143	1.164
Liver weight on body weight corrected for controls	-	107.8*	99.1	95.7	100.0
Kidney weight on body weight corrected for controls	-	112.3*	105.5	95.9	100.0
Blood urea nitrogen, mgm./100 ml.	-	22.40*	21.61*	19.96	17.89
Uninfected rats	16	11	8	6	13
Toxic deaths	16*	0	0	0	0
Mean no. of days to death	18*	-	-	-	-
Sets of tissues examined from uninfected rats	5	10	8	6	13
Sets with major pathology	5	1	0	0	0
Sets with any pathology	0	0	0	0	0

* Deviation from control is statistically significant

Of the 16 rats dosed in the group that received the highest concentration of "Cellosolve", 1.89 gm./kg./day, or 2.56% of the water, none survived for more than 38 doses, the mean number of days to death being 18. Their water and food consumption was statistically far below normal. The 5 animals from whom tissues were examined showed marked or general cloudy swelling of the kidney tubules and of the liver as well as excessive pigment deposition in the spleen. Three of these rats were male and these all showed complete lack of sperm in their testicles on micropathological examination. The same degree of kidney and liver damage seen in our treated animals was seen in our controls who succumbed later in the experiment to lung infection, however, none of the gross autopsies on the rats that received 1,888 gm./kg./day showed lung infection.

Eleven uninfected rats received 0.735 gm./kg./day and these showed statistically significant decrease in water and food consumption, in mean weight gain, body length and fatness of surviving rats, and significant increase in liver and kidney weight as well as in blood urea nitrogen. Tissues were examined on 3 male rats that succumbed and these all showed either immature or degenerated spermatic elements. Only one of the 5 deaths could not be accounted for by lung infection and no microscopic damage was reported for the rats that survived 90 doses.

Of the rats that received 0.213 and 0.052 gm./kg./day of "Cellosolve", none of 8 and of 6 respectively showed any microscopic, appetite, or growth damage as a result of their 90 doses. The blood urea nitrogen level of the 0.213 gm./kg./day group was slightly elevated but this is not considered significant as the kidney did not show micropathological injury in these rats. Therefore, the dosage level of 0.213 gm./kg./day is accepted as the highest concentration of "Cellosolve" tested that produced no effect.

Literature Cited

- (1) Morris, Herman J., Arthur A. Nelson and Herbert O. Calvery.
Observations on the chronic toxicities of propylene glycol, ethylene glycol, diethylene glycol, ethylene glycol mono-ethyl-ether, and diethylene glycol mono-ethyl-ether. J. Pharm. and Exper. Ther. 74: 266-273, 1942.

Carrol S. Weil

Carrol S. Weil

INDUSTRIAL FELLOW

Typed: September 4, 1947 - met

Table 10-250

Body Weight and Organ Weight at Sacrifice

gm./kg. (day)	Sex	Rat No.	Body Length in mm.	Body Weight in gm.	Fat- ness gm. per mm.	Liver Weight in gm.	Kidney Weight in gm.	Blood Urea N, mg%
0.735	M	51385	222	287	1.293	8.90	2.18	20.75
		51402	212	235	1.108	7.52	1.85	18.25
		51421	212	231	1.090	9.37	2.02	20.50
		51384	211	210	0.995	8.20	1.75	17.75
	F	51459	195	163	0.836	6.00	1.39	24.75
		51474	196	165	0.842	7.05	1.52	27.00
		51501	195	168	0.862	6.13	1.36	26.00
		51449	203	187	0.921	7.83	1.50	20.65
		51464	199	192	0.965	6.63	1.45	25.63
		51479	193	164	0.850	6.19	1.29	23.00
		51371	216	240	1.111	7.75	1.88	19.25
	F	51373	225	284	1.262	8.60	1.98	15.13
		51426	225	322	1.431	12.17	2.75	20.50
		51427	227	290	1.278	11.20	2.41	21.63
		51458	207	195	0.942	6.66	1.40	26.13
		51471	205	176	0.858	5.46	1.40	20.75
		51475	201	198	0.985	6.85	1.37	27.00
		51494	203	183	0.901	6.42	1.40	22.50
	0.052	M	51405	227	304	1.339	10.89	2.17
51414			233	311	1.335	11.70	2.38	17.13
F		51456	222	247	1.113	7.22	1.69	20.00
		51457	214	222	1.037	6.30	1.42	21.38
		51476	213	215	1.009	7.62	1.43	23.00
		51499	212	217	1.024	7.00	1.58	18.25
0.0	M	51391	228	335	1.469	11.75	2.50	23.75
		51425	226	255	1.128	8.38	1.80	18.63
		51439	230	300	1.304	10.65	2.31	19.25
		51374	230	349	1.517	13.20	2.57	16.00
		51441	238	337	1.416	12.32	2.38	19.75
	F	51455	212	197	0.929	6.93	1.50	17.38
		51482	215	231	1.074	7.49	1.61	14.75
		51487	214	224	1.047	7.66	1.50	13.75
		51498	210	224	1.067	7.43	1.65	20.75
		51463	206	224	1.087	7.15	1.50	15.50
		51477	210	218	1.038	7.58	1.61	18.63
		51509	206	209	1.014	7.62	1.99	18.63
		51510	212	222	1.047	7.41	1.68	15.75

Table 10-251

Growth, Fate, and Micropathology
(See abbreviations at end of table)

Age /kg. Sex	Rat No.	Weight at Start (gms.)	Weight Change (gms.)	Fate	Days to Fate	In- fection, etc.	Micropathology
0.88	M	51394	132	-	D	14	
		51410	112	-	D	15	
		51413	121	-	D	24	
		51430	134	-	D	18	
		51379	144	-	D	27	
		51380	146	-	D	38	
		51424	128	-	D	21	
	F	51434	108	-	D	17	
		51444	120	-	D	18	
		51448	125	-	D	14	
		51485	106	-	D	11	
		51508	104	-	D	16	
		51469	106	-	D	5	
		51472	117	-	D	19	
0.735	M	51493	118	-	D	18	
		51495	130	-	D	6	
		51376	129	-	D	76	LW
		51385	131	+ 156	S	90	
		51402	125	+ 110	S	90	
		51421	120	+ 111	S	90	
		51384	133	+ 77	S	90	
	F	51387	124	-	D	71	LW
		51392	120	-	D	75	LW
		51437	123	-	D	85	
		51459	102	+ 61	S	90	
		51474	129	+ 36	S	90	
		51477	136	-	D	69	LW
		51501	109	+ 59	S	90	
0.213	M	51449	122	+ 65	S	90	
		51464	120	+ 72	S	90	
		51479	112	+ 52	S	90	
		51490	104	-	K	71	Ear
	F	51371	117	+ 123	S	90	
		51373	135	+ 149	S	90	
		51426	144	+ 178	S	90	
51427		139	+ 151	S	90		
51458		116	+ 79	S	90		
51471		101	+ 75	S	90		
51475		127	+ 71	S	90		
51494	104	+ 79	S	90			

CONTINUED

Dosage in gm./kg. /day	Sex	Rat No.	Weight at Start (gms.)	Weight Change (gms.)	Fate	Days to Fate	In- fection, etc.	Micropathology
0.052	M	51405	112	+ 115	S	90		I, K, L, S, ST, T
		51414	120	+ 93	S	90		I, K, L, S, ST, T
		51422	122	-	D	77	LU	K, ICW, SG, ST, T
		51438	132	-	D	72	LU	KWX, ICW, Sg, ST, T
	F	51456	116	+ 131	S	90		I, K, L, S, ST
		51457	110	+ 112	S	90		I, K, L, S, ST
		51476	115	+ 100	S	90		I, K, L, S, ST
		51499	121	+ 96	S	90		I, K, L, S, ST
0.0	M	51391	133	+ 202	S	90		I, K, L, S, ST, T
		51399	156	-	D	83	LU	I, Kw, ICW, Sg, ST, T
		51425	120	+ 135	S	90		I, K, L, S, ST, T
		51439	122	+ 178	S	90		I, K, L, S, ST, T
		51372	116	-	D	87	LU	
		51374	124	+ 225	S	90		I, K, L, S, ST, T
		51396	140	-	D	20	LU	KWI, LUC, SG, ST
		51441	117	+ 200	S	90		I, K, L, S, ST, T
	F	51455	104	+ + 99	S	90		I, K, L, S, ST
		51482	104	+ 127	S	90		I, K, L, S, ST
		51487	114	+ 110	S	90		I, K, L, S, ST
		51498	114	+ 110	S	90		I, K, L, S
		51463	121	+ 103	S	90		I, K, L, ST
		51477	123	+ 95	S	90		I, K, L, S
		51509	108	+ 101	S	90		I, K, L, S, ST
		51510	113	+ 109	S	90		I, K, L, S, ST

Abbreviations

Mate

D = Died
K = Killed to protect cage mates
S = Sacrificed for examination

Infection, etc.

Eas = Middle ear infection
LJ = Lung infection seen grossly.

Micropathology

(Small letters indicate slight or scattered pathology.
capitals indicate marked or general pathology)

I = Intestine, normal

K = Kidney, normal

Kv = " , cloudy swelling of convoluted tubules
Kx = " , " " " loop tubules

L = Liver, normal

Lc = " , congested

Lg = " , free pigment

Lr = " , cloudy swelling

LUC = Lung, congested

S = Spleen, normal

Sg = " , excessive pigment

St = Stomach wall, normal

T = Testicle, normal

Tb = " , sperm absent

Ti = " , immature spermatid elements

Tx = " , degeneration of spermatid elements



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

William C. Kuryla, Ph.D.
Associate Director, Product Safety
Union Carbide Corporation
39 Old Ridgebury Road
Danbury, Connecticut 06817-0001

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

FEB 27 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12155A



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12

Triage of 8(e) Submissions

Date sent to triage: MAR 08 1995

NON-CAP

CAP

Submission number: 12155A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Marrosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

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Contractor reviewer :	<u>LPS</u>	Date:	<u>1/25/95</u>

CECATS DATA:

Submission # SEHO-0992-12155 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Union Carbide

Coccoloba

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0570 REFER TO CHEMICAL SCREENING
- 0578 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION OF WORKING STATUS
- 0404 LABELS/MSDS (CHANGES)
- 0405 PROCESSING/IN PROGRESS (CHANGES)
- 0406 APP/USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 09/22/92 09/29/92 CSRAD DATE: 12/01/94

CHEMICAL NAME:

Cellosolve

CASE

110-80-5

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MEDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAJE DATA	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	<u>YES</u>	YES (DROP/REFER)	<u>RAT</u>	LOW		
CAS SR	NO	NO (CONTINUE)		<u>MED</u>		
	IN PROGRESS	NO/PA		HIGH		

110-80-5 Rats received cellosolve in the drinking water for 90 days at the intake levels of 0, 0.052, 0.213, 0.735, 1.888 gm/kg/day. The highest level produced 100% mortality at the end of 38 doses and the next highest level produced significant effects on appetite, growth, organ weights. The higher dose animal showed kidney and liver damage. The 0.213 gm/kg/day was NOAEL.