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

September 24, 1992

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

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INIT

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 correspondence (with attachments) concerning the toxicology of Butyl CARBITOL® (Diethylene Glycol Monobutyl Ether; CASRN 112-34-5).

"Butyl CARBITOL®", Union Carbide Corp. letter from T. R. Tyler to C. A. Burger (Interstate Chemicals, Inc.), November 14, 1984 (with enclosed reports (7)).

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)

butcar

mm
5/1/95

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

November 14, 1984

BUTYL CARBITOL®

Mr. Charles A. Burger
Interstab Chemicals, Inc.
500 Jersey Avenue
P.O. Box 638
New Brunswick, New Jersey 08903

Dear Mr. Burger:

In your letter to Mr. Wise dated November 1, 1984, you requested studies we might have concerning adverse health effects of Butyl CARBITOL[®] (diethylene glycol monobutyl ether, DGBE). I enclose the following reports:

1. Mellon Institute of Industrial Research, Summary of the Toxicity of the Glycols and Their Derivatives. 14. Single Doses of Butyl CARBITOL by Skin Absorption. Dated 6/27/38.
2. Mellon Institute of Industrial Research, Summary of the Toxicity of the Glycols and Their Derivatives. 69. Single Doses of Butyl CARBITOL by Mouth to Rabbits. Dated 9/25/40.
3. Mellon Institute of Industrial Research, Summary of the Toxicity of the Glycols and Their Derivatives. 15. Single Doses of Butyl CARBITOL by Mouth. Dated 7/6/38.
4. Mellon Institute of Industrial Research, Summary of the Toxicity of the Glycols and Their Derivatives. 58. Single Doses by Skin Absorption of Butyl CARBITOL Acetate, CARBITOL Acetate, CELLOSOLVE Acetate, Methyl CARBITOL, Methyl CELLOSOLVE Acetate. Dated 1/20/40.
5. Thompson, E.D., Coppinger, W.J., Valencia, R. and Iavicoli, J. (1984). "Mutagenicity Testing of Diethylene Glycol Monobutyl Ether". Env. Health Persp., 57:105-112.
6. Schuler, R.L., Hardin, B.D., Niemeier, R.W., Booth, G., Hazelden, K., Piccirillo, V. and Smith, K. (1984). "Results of Testing Fifteen Glycol Ethers in a Short-Term In Vivo Reproductive Toxicity Assay". Env. Health Persp., 57:141-146.
7. Dugard, P.H., Walker, M., Mawdsley, S.J. and Scott, R.C. (1984). "Absorption of Some Glycol Ethers Through Human Skin In Vitro". Env. Health Persp., 57:193-197.

SUMMARY

-2-

We would also advise you that DGBE and DGBE are under consideration for mandatory testing by the EPA Test Rule Development Group. The outcome of their decision as to whether or not additional testing is required will evolve over the next several months.

I hope the accompanying information will be of some value to you. If you have any additional questions please feel free to call me.

Sincerely,

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Corporate Director
of Applied Toxicology



B-3

UNION CARBIDE CORPORATION OLD RIDGEBURY ROAD, DANBURY, CT 06817
Corporate Health, Safety and Environmental Affairs Department

November 14, 1984

BUTYL CARBITOL[®]

Mr. Charles A. Burger
Interstab Chemicals, Inc.
500 Jersey Avenue
P.O. Box 638
New Brunswick, New Jersey 08903

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I hope the accompanying information will be of some value to you. If you have any additional questions please feel free to call me.

Sincerely,

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Corporate Director
of Applied Toxicology

TRT/rjk
Encs.

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

SUMMARY OF THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES14. Single Doses of ~~XXXXXXXXXX~~ Butyl "Carbitol," and ~~XXXXXXXXXX~~ by Skin AbsorptionCarbide & Carbon Chemicals Corp. Industrial Fellowship No. 274-1

This summary of a more detailed report has been prepared for those who are not interested in a discussion of the methods and protocols of the work.

Skin applications were made by bandaging cotton pads saturated with measured volumes of the materials onto the clipped skin of guinea pigs, and leaving the application in place for four days. There is some uncertainty in the amount of the materials absorbed, since the cotton pads were still moist when removed, but there was little opportunity for evaporation, and no opportunity for the animal to obtain any of the material by mouth.

The results are:

Material	MLD (50% Level) By Skin Absorption	MLD (50% Level) By Mouth	Ratio of MLD's
XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX
Butyl "Carbitol"	2 "	2.0 "	100

Due to the uncertainty mentioned above, these MLD figures are not determined with the precision of the MLD figures by mouth. The pathology and symptoms of the injured animals were identical with those of animals fed by mouth.

The ratio of the MLD's by skin absorption and by mouth for a given material does not give the degree of skin absorption of the material, due to differences in absorption time by the two routes, but does give a value related to this absorption.

In attempting to extend these animal results to human applications, it must be remembered, (1) that guinea pigs have no sweat glands and thus, no doubt, absorb materials through the skin more slowly than do humans, (2) that the dosages applied here were enormous in comparison with any probable human application of the materials, and (3) that the doses were left on the animals four days, which is probably equivalent to 24 to 48 hours application to human skin.

Henry F. Smyth, Jr.

Jane Seston
Louise Leslie
June 29, 1938-mah


INDUSTRIAL FELLOW

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES

14. Single doses of [redacted], Butyl "Carbitol", and [redacted] by skin absorption

Carbide & Carbon Chemicals Corp. Industrial Fellowship No. 274-1

AFDR
Delayed
Death

This is the fourteenth report in a series, and the first of the series to discuss absorption of glycol derivatives through the skin. [redacted] has been included in the present report for the purpose of comparison.

Literature

The effect of single doses of [redacted] by mouth was covered in No. 8 of the present series, of [redacted] in No. 6, and that of Butyl "Carbitol" will be covered in a report to be issued shortly.

Nothing was found in the literature discussing the absorption of these three materials through the skin, although it is well known that many organic and some inorganic materials pass readily through the human or animal skin. Macht (1938) gives a review of this general question, together with much original work. Clark (1933) writes "The healthy epidermis is impervious to drugs. - - Probably any absorption that occurs through the skin occurs through these ducts." (i.e. through sweat glands and hair follicles). He further states that drugs in watery solutions are not absorbed, but drugs in lipid solvents may be absorbed. As soon as a drug reaches the dermis layer, it is picked up by the blood stream and is dispersed over the entire body.

Methods

Although albino rats are in many ways the most satisfactory animal for toxicological study, they cannot be used for any but the briefest skin absorption tests. It is impossible to hold a bandage on a rat without so restricting its freedom that its health suffers, and any direct application to the skin will be licked off rapidly unless its taste is very unpleasant. Therefore guinea pigs have been used in this study

Using electric clippers, the hair was removed from a band of skin about three inches wide, completely encircling the animal between the fore and hind legs. One day was then allowed for healing of any small accidental skin nicks. Then the animal was weighed, and the dose, calculated in terms of milliliters of material per kilo body weight. A piece of three-inch adhesive tape was cut, long enough to encircle the clipped area about twice. On this a flat pad of absorbent cotton was laid, thick enough and large enough to retain the entire calculated dose. For the larger doses this cotton pad was about two by ten centimeters, and the full thickness of cotton in a standard one pound roll. For smaller doses the pad was made proportionately smaller and thinner. This cotton pad then received the measured dose, and the tape and pad were wrapped about the pig, covering the clipped area, the cotton over the abdomen. After three, or in most cases four days, the tape was removed without the use of solvents, the skin area observed for signs of irritation other than that due to the tape, and the animal kept under observation for two weeks, or until it died.

The remarks in the first report of this series on statistical interpretation of results apply equally to this mode of administration of dosage.

Results

The results are tabulated below:

Material	MLD (50% level) by skin absorption	MLD (50% level) by mouth	Ratio of MLD through skin to MLD by mouth
Butyl "Carbitol"	2	2.0	100

Results with single dosages appear in Table 54, and with individual animals in Tables 55 to 58.

Table 54

"Carbitol", Butyl "Carbitol", and Glycerine

Summary of results with single doses by skin absorption.
Administered undiluted to mixed guinea pigs, on cotton poultices

Material	Dosage in ml./kg.	Pigs dosed	Mortality
Butyl "Carbitol"	4	5*	100
	2	10	50
	1	8	25
	0.5	8	25
	0.25	6	17
(MLD by mouth 2.0 gm./kg.)	0.10	6	17

* not in detailed tables

Symptoms and Gross Pathology

Gross pathology of animals killed by the applications did not differ from that of animals dosed with the same materials by mouth. After about 12 hours the animals became accustomed to the restriction of the bandage and ate and in general behaved as usual, those having large doses being weak, with low body temperature, perhaps passing into a coma, and dying; those with small doses apparently not being affected. Death in general was more delayed than with corresponding doses by mouth, but this is to be expected since absorption into the blood stream was slower. No evidence of skin irritation from the dose in the cotton pad was seen, although the animals obviously suffered considerable stinging and irritation when the doses were first applied.

Discussion

Since the guinea pig has no sweat glands in the skin, absorption of these doses was slower than would be the case with humans. A rough estimate would be that the four-day application to pigs is equivalent to about one day or at most two days application to human skin. Because of this slower absorption, results are not really comparable with results of administering single doses by mouth. In the latter case, most of the damage takes place within the first day, and the bulk of the dose is eliminated or destroyed in this time, while in skin absorption tests some new material is being added to the blood continually for four days. The results then are much more nearly comparable to the repeated doses so often used in therapeutics.

Another source of uncertainty in the results is that the cotton pads were always moist or wet with the material at the end of four days when they were removed, so the actual amount entering the system is unknown.

It was impossible for the animals to obtain any of the material applied by biting the bandage, and usually there were no signs of tooth marks on the edges of it. The tape adhered firmly to the clipped skin, and almost no cracks remained to allow seepage or evaporation of the dose. With more volatile materials it would of course be necessary to cover the cotton pad with an impervious film, as of tin foil, to prevent evaporation through the adhesive tape. None of the bandages were at all moist on the outside of the adhesive tape, so none of the fluids applied seeped through the tape.

Several years ago the Fellow made similar applications in which animals received control applications of water. In this past study it was found that the bandages could be left on thirty days without interfering with the growth of the animals. At the end of this time new bandages could be applied, and so long as bandages were renewed before the animals outgrew them, they remained normal.

Some of the uncertainties mentioned above account for the fact that the results with this method are more scattered than when doses are fed by mouth, and therefore the MLD's determined have a higher uncertainty. For this reason it has not been considered useful to convert the dosage expressed in ml./kg. to the same units as were used for doses by mouth; that is, gms./kg. In the glycol series, the difference between grams and milliliters is considerably less than the uncertainty of the toxicity determinations, so that no error is introduced by using the two units interchangeably.

It would be anticipated that lipid solubility would be accompanied by rapid skin absorption, and lipid insolubility by slow skin absorption, unless a material is sufficiently irritating to destroy skin cells and thus upset theoretical considerations. In the tabulation on Page 104, there appears

column giving the ratio of MLD by skin absorption to MLD by mouth. If there were no difference in the times of absorption between dosing by skin absorption and by mouth, then this column would indicate the portion of the total dose which was absorbed. Probably in any case the figures in this column do bear some relation to this portion absorbed. [REDACTED], with low lipid solubility, is seen to have a low absorption; Butyl "Carbitol" with relatively high lipid solubility, is seen to have a high skin absorption; and the [REDACTED] present in [REDACTED] having a relatively low lipid solubility, apparently decreases the absorption of this grade of [REDACTED] when it is compared with the glycol-free grade.

In attempting to extend these animal results to human applications of these materials, it must be remembered, (1) that guinea pigs have no sweat glands and thus no doubt absorb materials through the skin more slowly than do humans, (2) that the dosages applied here were enormous in comparison with any probable human application of the materials, and (3) that the doses were left on the animals four days, which is probably equivalent to 24 or 48 hours' application to human skins.

Henry F. Smyth, Jr.

Jane Seaton
Louise Leslie


INDUSTRIAL FELLOW

Literature cited

- Clark, A. J. (1933) Applied Pharmacology, 5th Edition, J. A. Churchill, London.
Macht, D. I. (1938) The absorption of drugs and poisons through the skin and mucous membranes, Jour. Amer. Med. Assoc. 110, 409-414, February 5.

Table 57

Butyl "Carbitol"

Single doses to mixed guinea pigs, by skin absorption
Administered undiluted on cotton poultices.

Pig No.	Sex	Date Clipped	Date Dosed	Date Poultice Removed	Grams Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
996	M	5-9-38	5-10	5-14	212		2	0.42	14
997	M	5-9	5-10	5-14	214		2	0.43	6
1225	M	6-6	6-7	6-11	248		2	0.50	13
1226	M	6-6	6-7	-	224		2	0.45	3
1155a	F	5-24	5-26	5-30	252		2	0.55	10
1227	M	6-6	6-7	6-11	174	+ 38	2	0.35	-
1228	M	6-6	6-7	6-10	263	- 9	2	0.53	-
1229	M	6-6	6-7	6-10	261	+ 34	2	0.52	-
1154a	F	5-24	5-26	5-30	180	+ 12	2	0.36	-
1156a	F	5-24	5-26	5-30	197	+ 8	2	0.39	-
1232	M	6-6	6-7	6-11	220		1	0.22	6
998	F	5-9	5-10	5-14	262		1	0.26	6
1230	M	6-6	6-7	6-11	200	+ 34	1	0.20	-
1231	M	6-6	6-7	6-11	176	+ 24	1	0.18	-
1233	M	6-6	6-7	6-11	248	- 4	1	0.25	-
1234	M	6-6	6-7	6-11	252	+ 20	1	0.25	-
1157a	F	5-24	5-26	5-30	186	- 2	1	0.19	-
1158a	F	5-24	5-26	5-30	238	0	1	0.24	-
1000	M	5-9	5-10	5-14	200		0.5	0.10	13
1001	F	5-9	5-10	5-14	244		0.5	0.12	13
1159a	M	5-24	5-26	5-30	270	- 52	0.5	0.14	-
1160a	M	5-24	5-26	5-30	270	- 12	0.5	0.14	-
1161a	M	5-24	5-26	5-30	224	+ 13	0.5	0.11	-
1235	M	6-6	6-7	6-11	230	+ 16	0.5	0.12	-
1236	M	6-6	6-7	6-11	252	+ 24	0.5	0.13	-
1237	M	6-6	6-7	6-11	218	+ 26	0.5	0.11	-
1159b	F	6-1	6-2	6-6	244		0.25	0.06	12
1157b	M	6-1	6-2	6-6	238	- 18	0.25	0.07	-
1160b	M	6-1	6-2	6-6	221	+ 31	0.25	0.06	-
1161b	M	6-1	6-2	6-6	233	-29	0.25	0.06	-
1276	M	6-10	6-11	6-15	268	- 12	0.25	0.07	-
1158b	F	6-1	6-2	6-6	248	- 19	0.025	0.06	-
1166	M	6-1	6-2	6-6	230	+ 14	0.1	0.02	4
1162	M	6-1	6-2	6-6	258	- 14	0.1	0.03	-
1163	M	6-1	6-2	6-6	238	- 16	0.1	0.02	-
1164	M	6-1	6-2	6-6	224	+ 10	0.1	0.02	-
1165	M	6-1	6-2	6-6	222	- 24	0.1	0.02	-
1167	M	6-1	6-2	6-6	230	+ 14	0.1	0.02	-

Confidential

R: 9-25-40

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MELLON INSTITUTE OF INDUSTRIAL RESEARCH

University of Pittsburgh

SPECIAL REPORT

on

SUMMARY OF THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES

69. Single Doses of Butyl "Carbitol" by Mouth to Rabbits

Carbide & Carbon Chemicals Corporation Industrial Fellowship No. 274-3

The more important materials being studied are fed to rabbits as well as to rats and guinea pigs to increase the validity of the results by data from a third species. Rabbits are not purchased for this use alone, but are used for doses by mouth only after eyes and skin have been used on other tests. The most recent material fed to rabbits is butyl "Carbitol."

The sample was of the usual commercial grade and was shipped from South Charleston late in 1937 in package S-70693. It is the same sample that was fed to rats and guinea pigs, as described in report fifteen of this series dated 7-6-38.

The LD₅₀ for rats was found to be 6.5 gm/kg. and for guinea pigs 2.0 gm/kg. The LD₅₀ for rabbits, 2.5 gm/kg., indicates this species to be slightly less sensitive to butyl "Carbitol" than are guinea pigs. The same relation was found with "Carbitol" and ethylene glycol.

Henry F. Smyth, Jr.


SENIOR INDUSTRIAL FELLOW

September 25, 1940-mah

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES69. Single Doses of Butyl "Carbitol" by Mouth to RabbitsCarbide & Carbon Chemicals Corporation Industrial Fellowship No. 274-3

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The sample was of the usual commercial grade, and was shipped from S. Charleston late in 1937 in package S-70693. It is the same sample that was fed to rats and guinea pigs as described in Report 15 of this series dated 7-6-38.

Results

The results are summarized in Table 248 and presented in more detail in Table 249.

Table 248Butyl "Carbitol"Summary of Single Doses by mouth to Albino Rabbits

<u>Dosage, gm/kg</u>	<u>Rabbits Dosed</u>	<u>Mortality</u>
4.0	6*	100 %
3.0	10	70
2.5	10	20
2.0	10	20
1.5	6*	0
	LD ₀	1.5 gm/kg
	LD ₅₀	2.5 gm/kg
	LD ₁₀₀	4.0 gm/kg

* Not in Table 249

Discussion

The LD₅₀ for rats was found to be 6.5 gm/kg and for guinea pigs 2.0 gm/kg. The LD₅₀ for rabbits, 2.5 gm/kg, indicates this species to be slightly less sensitive to Butyl "Carbitol" than are guinea pigs. The same relation was found with "Carbitol" and Ethylene Glycol.

Henry F. Smyth, Jr.—abc


SENIOR INDUSTRIAL FELLOW

September 25, 1940

Table 249

Butyl "Carbitol"

Single Doses to Mixed Albino Rabbits

Administered by somach tube as solution in water, 1 ml. = 0.10 or 0.20 grams

Rabbit No.	Date Dosed	Grams Wt.	Weight Change in 14 Days	Dosage; Grams Per Kilo	Dose in Grams	Dose in ml. of Solution	Days to Death
296	5-3-40	1830	-	3.0	5.50	27.5	3
297	5-10	2340	-	3.0	7.00	35.0	1
299	5-3	1662	-	3.0	5.00	25.0	1
304	5-10	1778	-	3.0	5.34	26.7	1
305	5-3	1886	-	3.0	5.64	28.2	1
311	5-10	1622	-	3.0	4.87	24.4	3
313	5-3	1727	-	3.0	5.98	29.9	1
300	5-3	1690	- 62	3.0	5.06	25.3	-
307	5-3	1814	+ 267	3.0	5.44	27.2	-
310	5-3	1692	+ 337	3.0	5.08	25.4	-
291	5-3	2187	-	2.5	5.48	54.8	1
322	6-14	2095	-	2.5	5.23	26.2	1
274	3-29	2054	+ 155	2.5	5.13	51.3	-
275	3-29	1705	+ 210	2.5	4.26	42.6	-
290	4-12	1440	+ 203	2.5	3.60	36.0	-
293	4-24	2602		2.5	6.50	65.0	-
294	4-12	1919	+ 366	2.5	4.80	48.0	-
295	4-12	1360	+ 409	2.5	3.40	34.0	-
306	4-24	1571	+ 489	2.5	3.92	39.2	-
309	4-24	1540	+ 254	2.5	3.85	38.5	-
260	2-16	1876	-	2.0	3.75	37.5	3
301	4-24	1442	-	2.0	2.88	28.8	6
261	2-16	1984	+ 301	2.0	3.96	39.6	-
268	2-29	2073		2.0	4.15	41.5	-
269	3-9	2144	+ 425	2.0	4.30	43.0	-
272	3-9	2082	+ 381	2.0	4.17	41.7	-
276	3-22	1994		2.0	4.00	40.0	-
280	3-22	2182	+ 269	2.0	4.37	43.7	-
302	4-24	1362	+ 302	2.0	2.72	27.2	-
303	4-24	1530	+ 314	2.0	3.06	30.6	-

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

SUMMARY OF THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES

15. Single Doses of Butyl "Carbitol" by Mouth

Carbide & Carbon Chemicals Corporation Industrial Fellowship No. 274-1

This summary of a more detailed report has been prepared for those who are not interested in a discussion of the methods and protocols of the work.

The methods used were identical with those already described in earlier numbers of the series.

The minimum lethal dose (MLD, killing 50% of those receiving it) for guinea pigs by mouth was 2.0 grams per kilo body weight, and for rats was 6.5 grams per kilo. The MLD of a specially purified glycol-free sample was calculated to be 7.0 grams per kilo for rats, based on the feeding of one dosage to 20 animals, and the use of the curve obtained for the commercial grade.

There was nothing distinctive in the symptoms of injury from Butyl "Carbitol", but the narcotic effect of large doses was marked, and deaths of guinea pigs were delayed considerably. Both of these effects have been met before.

Henry F. Smyth Jr.
Jane Seaton
Louise Leslie

Henry F. Smyth Jr.
INDUSTRIAL FELLOW

July 7, 1938:LS

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES15. Single Doses of Butyl "Carbitol" by MouthCarbide & Carbon Chemicals Corp. _____ Industrial Fellowship No. 274-1AFDR
Delayed
Detail ✓

This is the fifteenth report in a series. The first of the series discussed the methods used.

Literature

No reference to the physiological effect of Butyl "Carbitol" has been found in the literature. Since Butyl Alcohol is more toxic than Ethyl Alcohol in single doses, it would be expected that this butyl ether would be more toxic than "Carbitol." Von Oettingen and Jirouch (1931) reported Butyl "Cellosolve" to be more toxic than "Cellosolve," supporting this assumption.

Methods

The material used for this study was shipped from the donor's plant in drum S-70693. In addition, there was used a special sample of Butyl "Carbitol" substantially free from Ethylene Glycol and other impurities. This was shipped from the donor's plant April 9, 1938, and was stated to be a weir sample taken during a plant distillation, and to contain $1.0 \pm 0.3\%$ Ethylene Glycol.

The methods of the work were covered in the first report of the series.

Results

The MLD of Butyl "Carbitol" as marketed was found to be 2.0 gms./kg. for guinea pigs, and 6.5 gms./kg. for rats. The special low-gravity sample had an MLD for rats of 7.0 gms./kg. based on administration of a single dosage and the form of the curve for commercial material. The results with single dosages are shown in Table 59, and with single animals in Tables 60 to 62.

Table 59

Butyl "Carbitol"

Summary of results with single dosages by mouth.
Fed by stomach tube as dilution in water, 1 ml. = 0.50 gram
for rats, 1 ml. = 0.10 gram for guinea pigs.

	Dosage in gms./kg.	<u>Male Albino Rats</u>		<u>Mixed Guinea Pigs</u>	
		<u>Rats</u> Dosed	Mortality.	<u>Pigs</u> Dosed	Mortality
A. Commercial grade	10	4	100%		
	8	10	50	4*	100%
	6	10	60	4*	100
	5	10	20	2*	100
	4			2*	100
	3	4	0	2*	100
	2.5			10	80
	2			10	70
	1.8			10	10
	1.5			10	20
	1.2			3*	0
	1			3*	0
	MLD (50% level)	6.5 gms./kg.		2.0 gms./kg.	
B. Low Gravity	6.5	20	35%		

*Not in detailed tables

Symptoms and Gross Pathology

Symptoms and gross pathology did not differ from those reported for

other glycol derivatives. The narcotic effect of large doses was marked, as it has been with all the glycol ethers. The deaths of fatally injured guinea pigs was quite delayed, as it has been with other diethylene glycol ethers.

Discussion

It is evident that Butyl "Carbitol" is considerably more toxic in single doses than is "Carbitol" or Methyl "Carbitol," and that the low gravity grade is slightly less toxic. This latter fact must be due to removal of unidentified toxic impurities in preparation of the sample, since it is illogical to believe that simply removal of Ethylene Glycol (having an MLD of 9.0 to rats) would decrease the toxicity.

Henry F. Smyth, Jr.


INDUSTRIAL FELLOW

Jane Seaton
Louise Leslie

July 7, 1938-mah

Literature Cited

Von Oettingen, W. F., and Jirouch, E. A., 1931; The Pharmacology of Ethylene Glycol, etc., J. Pharm. and Exper. Ther. 52, 355-372.

Table 60

Butyl "Carbitol"

Single doses to male rats, by mouth.
Fed by stomach tube, as dilution in water, 1 ml. = 0.50 gm.

Rat No.	Date Dosed	Grams Weight	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Grams	Dose in ml. of Dilution	Days to Death	Autopsy Made
653	3-2-38	140		10	1.40	2.8	1	x
654	3-2	112		10	1.12	2.2	1	x
655	3-2	100		10	1.00	2.0	2	-
656	3-2	110		10	1.10	2.2	1	x
958	3-30	86		8	0.69	1.4	1	-
959	3-30	112		8	0.89	1.8	1	-
961	3-30	108		8	0.86	1.7	2	-
1040	4-7	124		8	0.99	2.0	6	-
1041	4-7	116		8	0.93	1.85	1	-
954	3-30	1.16	+ 16	8	0.92	1.85	-	-
955	3-30	124	+ 20	8	0.99	2.0	-	-
960	3-30	108	+ 27	8	0.86	1.7	-	-
1038	4-7	126	0	8	1.01	2.0	-	-
1039	4-7	116	- 2	8	0.93	1.85	-	-
956	3-30	108		6	0.65	1.3	7	-
957	3-30	98		6	0.59	1.2	1	-
964	3-30	106		6	0.64	1.3	1	x
965	3-30	106		6	0.84	1.3	1	x
1042	4-7	104		6	0.62	1.25	1	-
1045	4-7	102		6	0.61	1.2	1	-
962	3-30	116	+ 20	6	0.70	1.4	-	-
963	3-30	116	+ 11	6	0.70	1.4	-	-
1043	4-7	86	+ 24	6	0.52	1.0	-	-
1044	4-7	118	+ 12	6	0.71	1.4	-	-
830	4-13	182		5	0.91	1.8	1	-
833	4-13	138		5	0.69	1.4	1	-
657	3-2	124	+ 47	5	0.62	1.25	-	-
658	3-2	104	+ 17	5	0.52	1.05	-	-
659	3-2	118	+ 19	5	0.59	1.2	-	-
660	3-2	112	+ 20	5	0.56	1.1	-	-
1046	4-7	112	+ 8	5	0.56	1.1	-	-
1047	4-7	114	+ 12	5	0.57	1.15	-	-
1048	4-7	106	- 4	5	0.53	1.05	-	-
1049	4-7	94	+ 14	5	0.47	0.95	-	-

Table 61

Butyl "Carbitol," Low-Gravity

Single doses to male rats, by mouth.
Fed by stomach tube as dilution in water, 1 ml. = 0.50 gm.

Rat No.	Date Dosed	Grams Weight	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Grams	Dose in ml. of Dilution	Days to Death
1567	6-2-38	112		6.5	0.73	1.45	3
1568	6-2	110		6.5	0.72	1.45	1
1575	6-2	84		6.5	0.55	1.10	1
1726	6-20	96		6.5	0.62	1.30	1
1727	6-20	114		6.5	0.74	1.50	1
1730	6-20	110		6.5	0.72	1.45	1
1732	6-20	96		6.5	0.62	1.25	1
1566	6-2	112	+ 67	6.5	0.73	1.45	-
1569	6-2	124	+ 40	6.5	0.80	1.60	-
1570	6-2	128	+ 57	6.5	0.83	1.65	-
1571	6-2	104	+ 57	6.5	0.68	1.35	-
1572	6-2	116	+ 51	6.5	0.75	1.50	-
1573	6-2	122	+ 54	6.5	0.79	1.60	-
1574	6-2	122	+ 43	6.5	0.79	1.60	-
1724	6-20	112	+ 24	6.5	0.73	1.45	-
1725	6-20	130	- 22	6.5	0.84	1.70	-
1728	6-20	102	+ 34	6.5	0.66	1.30	-
1729	6-20	128	- 33	6.5	0.83	1.65	-
1731	6-20	132	+ 9	6.5	0.84	1.70	-
1733	6-20	1.24	+ 5	6.5	0.80	1.60	-

Table 62

Butyl "Carbitol"

Single doses to mixed guinea pigs, by mouth.
Fed by stomach tube as dilution in water, 1 ml. = 0.10 gm.

Pig No.	Sex	Date Dosed	Grams Weight	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Grams	Dose of Dilution	Days to Death
1021	M	5-13-38	208		2.5	0.52	5.2	1
1026	M	5-13	252		2.5	0.63	6.3	10
1027	M	5-13	242		2.5	0.605	6.05	1
1024	M	5-13	200		2.5	0.50	5.0	10
1029	M	5-13	244		2.5	0.61	6.1	7
1030	M	5-13	230		2.5	0.575	5.75	1
1022	F	5-13	234		2.5	0.585	5.85	1
1023	F	5-13	244		2.5	0.61	6.1	1
1028	M	5-13	226	- 7	2.5	0.565	5.65	-
1025	F	5-13	224	+ 4	2.5	0.56	5.6	-
599	M	3-28	228		2	0.46	4.6	7
600	M	3-28	171		2	0.34	3.4	2
972	M	5-5	226		2	0.67	6.7	6
1018	M	5-13	224		2	0.45	4.5	10
971	F	5-5	320		2	0.64	6.4	11
1017	F	5-13	230		2	0.46	4.6	10
1019	F	5-13	200		2	0.40	4.0	1
970	M	5-5	354	- 54	2	0.71	7.1	-
1016	M	5-13	224	+ 18	2	0.45	4.5	-
1020	M	5-13	234	+ 1	2	0.47	4.7	-
981	M	5-5	292		1.8	0.53	5.3	1
973	M	5-5	254	- 22	1.8	0.46	4.6	-
974	M	5-5	322	- 54	1.8	0.58	5.8	-
976	M	5-5	248	- 96	1.8	0.63	6.3	-
979	M	5-5	344	- 4	1.8	0.62	6.2	-
975	F	5-5	302	- 2	1.8	0.54	5.4	-
977	F	5-5	302	- 2	1.8	0.54	5.4	-
978	F	5-5	276	- 6	1.8	0.50	5.0	-
980	F	5-5	244	- 4	1.8	0.44	4.4	-
982	F	5-5	250	- 32	1.8	0.45	4.5	-
967	M	5-5	284		1.5	0.43	4.3	12
969	M	5-5	210		1.5	0.315	3.15	11
813	M	4-14	236	- 16	1.5	0.35	3.5	-
815	M	4-14	258	- 32	1.5	0.39	3.9	-
1204	M	6-6	232	+ 18	1.5	0.35	3.5	-
1205	M	6-6	200	- 2	1.5	0.30	3.0	-
814	F	4-14	204	+ 23	1.5	0.31	3.1	-
1201	F	6-6	228	- 83	1.5	0.33	3.3	-
1202	F	6-6	216	- 12	1.5	0.32	3.2	-
1203	F	6-6	208	- 4	1.5	0.31	3.1	-

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

SUMMARY OF THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES58. Single Doses by Skin Absorption of Butyl "Carbitol" Acetate, "Carbitol" Acetate, "Cellosolve" Acetate, Methyl "Carbitol," Methyl "Cellosolve" AcetateAFIDR
Delayed
DeathCarbide & Carbon Chemicals Corp. Industrial Fellowship No. 274-3

Most of the data presented in this report are not satisfactory quantitatively, and the report is issued only for the purposes of record.

The results on the five materials are listed below. In most cases these are only approximations.

<u>Material</u>	<u>LD50</u>
Butyl "Carbitol" Acetate	Indeterminate between 20 and 50 gm/kilo
"Carbitol" Acetate	Indeterminate but above 30 gm/kilo
Methyl "Carbitol"	8 gm/kilo
"Cellosolve" Acetate	Approximately 20 gm/kilo
Methyl "Cellosolve" Acetate	10 gm/kilo

These data illustrate the experience of the Fellowship with the skin absorption method when applied to materials of low toxicity. The difficulty is the uncertain contact of large doses with guinea pig skin. It is concluded that this method is unsatisfactory when the LD50 is above 5 grams/kilo. Since the LD50's of the five materials covered in the present report are all above 5, they are quantitatively invalid and one can simply say that these five materials have relatively low toxicity when applied to the skin. No further determinations will be made of skin absorption toxicity unless preliminary trials show the LD50 to be less than 5 grams/kilo.

It is felt that this decision is practical, in that it is inconceivable that a human could receive single doses on the skin of 5 grams/kilo which would remain in place long enough for absorption. It certainly appears impossible to make applications of this magnitude to an experimental animal.

Henry F. Smyth, Jr.

SENIOR INDUSTRIAL FELLOW

R: 1-20-40

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MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

THE TOXICITY OF THE GLYCOLS AND THEIR DERIVATIVES58. Single Doses by Skin Absorption of Butyl "Carbitol" Acetate,
"Carbitol" Acetate, "Cellosolve" Acetate, Methyl "Carbitol," Methyl "Cellosolve" AcetateCarbide & Carbon Chemicals Corp. Industrial Fellowship No. 274-3

Most of the data presented in this report are not satisfactory quantitatively, and the report is issued only for the purposes of record.

Methods

Methods were discussed in report 14 of this series dated June 29, 1938. The only addition is that tin foil was used outside the application for the more volatile materials to reduce loss by vaporization. Samples were the regular commercial grades sold by the chemical company, except in the case of Butyl "Carbitol" Acetate, which was prepared for this work by Fellowship 155 in 1938.

Results

The results are summarized in Table 207 and presented in more detail in Tables 208-212. These results in most cases are only approximations and are listed most briefly below.

<u>Material</u>	<u>LD50</u>
Butyl "Carbitol" Acetate	Indeterminate between 20 and 50 gm/kilo
"Carbitol" Acetate	Indeterminate but above 30 gm/kilo
Methyl "Carbitol"	8 gm/kilo
"Cellosolve" Acetate	Approximately 20 gm/kilo
Methyl "Cellosolve" Acetate	10 gm/kilo

Table 207

Summary of results with single doses by skin absorption
Administered undiluted to mixed guinea pigs on cotton poultices

Material	Dosage in Ml/kg.	Pigs Dosed	Mortality
Butyl "Carbitol" Acetate	50	10	50%
	40	10	50
	20	10	50
	10	10	30
	8	10	30
	6	4	0
"Carbitol" Acetate	30	10	40%
	20	4	25
	15	8	12
	10	12	33
	5	10	20
"Cellosolve" Acetate with tin foil protection	50	4	100%
	20	10	60
	15	4	0
Methyl "Carbitol"	30	4*	100%
	20	10	70
	10	10	40
	5	10	60
	3	4*	25
	1	8*	38
Methyl "Cellosolve" Acetate with tin foil protection	20	4*	100%
	15	10	40
	10	10	60
	5	10	30

*Not in detailed tables

Discussion

These data illustrate the experience of the Fellowship with the skin absorption method when applied to materials of low toxicity. The difficulty is the uncertain contact of large doses with guinea pig skin. It is concluded that this method is unsatisfactory when the LD₅₀ is above 5 grams/kilo. Since the LD₅₀'s of the five materials covered in the present report are all above 5,

352.

they are quantitatively invalid and one can simply say that these five materials have relatively low toxicity when applied to the skin. No further determinations will be made of skin absorption toxicity unless preliminary trials show the LD₅₀ to be less than 5 grams/kilo.

It is felt that this decision is practical, in that it is inconceivable that a human could receive single doses on the skin of 5 grams/kilo which would remain in place long enough for absorption. It certainly appears impossible to make applications of this magnitude to an experimental animal.

Henry F. Smyth, Jr.


SENIOR INDUSTRIAL FELLOW

January 23, 1940-mah

Table 208

Butyl "Carbitol" Acetate

Single doses to mixed guinea pigs, by skin absorption
Administered undiluted on cotton poultices

Pig No.	Sex	Date Clipped	Date Dosed	Date Poultice Removed	Grams Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
3901	M	12-1-38	12-2		244		50	9.7	4
3667	F	11-10	11-11		218		50	10.9	3
3669	F	11-10	11-11	11-15	236		50	11.8	5
3983	F	12-15	12-16	12-20	224		50	11.2	7
3984	F	12-15	12-16	12-20	217		50	10.8	4
3898	M	12-1	12-2	12-6	294	- 31	50	14.7	-
3899	M	12-1	12-2	12-6	256	- 13	50	12.8	-
3982	M	12-15	12-16	12-20	220	+ 28	50	11.0	-
3665	F	11-10	11-11	11-15	236	- 38	50	11.8	-
3981	F	12-15	12-16	12-20	224	+ 8	50	11.2	-
3671	M	11-10	11-11	11-15	232		40	9.3	6
3673	M	11-10	11-11		228		40	9.1	3
3990	M	12-15	12-16		258		40	10.3	3
3985	F	12-15	12-16	12-20	221		40	8.8	8
3988	F	12-15	12-16	12-20	232		40	9.3	10
3986	M	12-15	12-16	12-20	221		40	8.8	-
3987	M	12-15	12-16	12-20	260		40	10.4	-
-3672	F	11-10	11-11	11-15	248	- 58	40	9.9	-
3674	F	11-10	11-10	11-15	232	- 66	40	9.3	-
3989	F	12-15	12-16	12-20	232	+ 4	40	9.3	-
3777	M	11-25	11-26	11-30	280		20	5.6	12
3779	M	11-25	11-26	11-30	275		20	4.5	5
3778	F	11-25	11-26		192		20	3.85	2
3780	F	11-25	11-26		235		20	4.7	3
3994	F	12-15	12-16	12-20	228		20	4.6	8
3781	M	11-25	11-26	11-30	274	- 33	20	5.5	-
3991	M	12-15	12-16	12-20	239	- 29	20	4.8	-
3995	M	12-15	12-16	12-20	263	- 3	20	5.3	-
3992	F	12-15	12-16	12-20	236	+ 17	20	4.7	-
3993	F	12-15	12-16	12-20	215	+ 14	20	4.3	-

(Continued)

Table 208 Cont'd

Pig No.	Sex	Date Clipped	Date Dosed	Date Poultrice Removed	Grams Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
3998	M	12-15	12-16	12-20	197		10	2.0	8
4153	M	1-5-39	1-6	1-10	244		10	2.4	10
4154	F	1-5	1-6	1-10	236		10	2.4	10
3996	M	12-15-38	12-16	12-20	252	+ 20	10	2.5	-
3997	M	12-15	12-16	12-20	225	+ 50	10	2.3	-
4009	M	12-15	12-16	12-20	249	- 9	10	2.5	-
4155	M	1-5-39	1-6	1-10	223	+ 17	10	2.2	-
4156	M	1-5	1-6	1-10	154	+ 54	10	1.5	-
3999	F	12-15-38	12-16	12-20	229	+ 26	10	2.3	-
4152	F	1-5-39	1-6	1-10	239	- 15	10	2.3	-
4157	M	1-5	1-6	1-10	227		8	1.8	7
4158	F	1-5	1-6	1-10	280		8	2.2	4
4270	F	1-19	1-20	1-24	233		8	1.9	13
4160	M	1-5	1-6	1-10	235	+ 19	8	1.9	-
4269	M	1-19	1-20	1-24	240	+ 12	8	1.9	-
4273	M	1-19	1-20	1-24	271	+ 13	8	2.2	-
4274	M	1-19	1-20	1-24	235	+ 19	8	1.9	-
4159	F	1-5	1-6	1-10	258	- 26	8	2.1	-
4271	F	1-19	1-20	1-24	312	- 12	8	2.5	-
4272	F	1-19	1-20	1-24	248	- 28	8	2.0	-
4444	M	2-9	2-10	2-14	250	- 17	6	1.5	-
4442	F	2-9	2-10	2-14	255	- 27	6	1.5	-
4443	F	2-9	2-10	2-14	246	- 14	6	1.5	-
4445	F	2-9	2-10	2-14	235	- 20	6	1.4	-

Table 209

"Carbitol" Acetate

Single doses to mixed guinea pigs, by skin absorption
Administered undiluted on cotton poultices

Pig No.	Sex	Date Clipped	Date Dosed	Date Poultice Removed	Grams Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
4382	M	2-2-39	2-3	2-7	215		30	6.5	14
4385	M	2-2	2-3	2-7	254		30	7.6	5
4383	F	2-2	2-3	2-7	253		30	7.6	5
4388	F	2-2	2-3	2-7	291		30	8.7	11
4384	M	2-2	2-3	2-7	275	- 13	30	8.3	-
4161	F	1-5	1-6	1-10	221	- 29	30	6.6	-
4162	F	1-5	1-6	1-10	232	+ 10	30	7.0	-
4164	F	1-5	1-6	1-10	288	+ 46	30	8.7	-
4386	F	2-2	2-3	2-7	243	+ 46	30	7.3	-
4387	F	2-2	2-3	2-7	256	- 41	30	7.7	-
4077	F	12-29-38	12-30	1-3	232		20	4.6	14
4076	M	12-29	12-30	1-3	280	- 19	20	5.6	-
4075	F	12-29	12-30	1-3	226	- 30	20	4.5	-
4078	F	12-29	12-30	1-3	224	- 1	20	4.5	-
3796	M	11-25	11-26		224		15	3.4	2
4071	M	12-29	12-30	1-3	281	- 13	15	4.2	-
4073	M	12-29	12-30	1-3	308	- 19	15	4.6	-
4074	M	12-29	12-30	1-3	248	- 40	15	3.7	-
3793	F	11-25	11-26	11-30	244	0	15	3.7	-
3794	F	11-25	11-26	11-30	242	- 4	15	3.6	-
3795	F	11-25	11-26	11-30	218	+ 31	15	3.3	-
4072	F	12-29	12-30	1-3	272	- 42	15	4.1	-
3792	M	11-25	11-26		264		10	2.6	2
3727	F	11-17	11-18		212		10	2.1	3
3789	F	11-25	11-26		204		10	2.0	2
4001	F	12-15	12-16	12-20	208		10	2.1	5
3725	M	11-17	11-18	11-22	308	- 64	10	3.1	-
4003	M	12-15	12-16	12-20	237	+ 8	10	2.4	-
3724	F	11-17	11-18	11-22	245	+ 8	10	2.45	-
3726	F	11-17	11-18	11-22	216	+ 6	10	2.2	-
3790	F	11-25	11-26	11-30	214	+ 38	10	2.1	-
3791	F	11-25	11-26	11-30	238	- 7	10	2.4	-
4000	F	12-15	12-16	12-20	238	+ 30	10	2.4	-
4002	F	12-15	12-16	12-20	228	- 16	10	2.3	-

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Table 209 Cont'd

Pig No.	Sex	Date Clipped	Date Dosed	Date Moulting Removed	Grams Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
3731	M	11-17	11-18	11-22	224		5	1.1	7
4006	M	12-15	12-16	12-20	255		5	1.3	6
3729	M	11-17	11-18	11-22	272	- 46	5	1.4	-
4005	M	12-15	12-16	12-20	260	+ 44	5	1.3	-
4007	M	12-15	12-16	12-20	304	+ 36	5	1.5	-
4008	M	12-15	12-16	12-20	254	- 2	5	1.3	-
3728	F	11-17	11-18	11-22	200	+ 20	5	1.0	-
3730	F	11-17	11-18	11-22	246	+ 44	5	1.2	-
4004	F	12-15	12-16	12-20	276	- 36	5	1.4	-
4165	F	1-5-39	1-6	1-10	272	+ 35	5	1.4	-

357.

Table 210

"Cellosolve" Acetate

Single Doses to Mixed Guinea Pigs by Skin Absorption
Administered undiluted on cotton poultices with tin foil protection

Pig No.	Sex	Date Clipped	Date Dosed	Date Poultrice Re-moved	Grams Wt.	Weight Change in 14 Days	Dosage; ml per Kilo	Dose in Ml.	Days to Death
5537	M	9-6-39	9-7	-	230	-	50	11.5	2
5538	M	"	"	-	243	-	50	12.2	2
5535	F	"	"	-	239	-	50	12.0	2
5536	F	"	"	-	210	-	50	10.5	2
5531	M	9-6	9-7	-	270	-	20	5.4	4
5532	M	"	"	9-11	269	-	20	5.4	5
5533	F	"	"	-	239	-	20	4.8	4
5534	F	"	"	-	246	-	20	4.9	2
5586	F	9-14	9-15	9-19	236	-	20	4.7	8
5589	F	"	"	9-19	259	-	20	5.2	8
5471	F	8-24	8-26	8-30	244	+ 38	20	4.9	-
5473	F	"	"	8-30	258	+ 18	20	5.2	-
5587	F	9-14	9-15	9-19	264	- 24	20	5.3	-
5588	F	"	"	9-19	271	- 59	20	5.4	-
5466	M	8-24	8-26	8-30	264	+ 13	15	4.0	-
5467	M	"	"	"	239	+ 11	15	3.6	-
5468	M	"	"	"	235	+ 1	15	3.5	-
5469	F	"	"	"	238	- 26	15	3.6	-

Table 211

Methyl "Carbitol"

Single Skin Applications to Mixed Guinea Pigs
Applied Undiluted on Cotton Poultices

Pig No.	Sex	Date Clipped	Date Dosed	Date Poul-tice Removed	Grams Wt.	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Ml.	Days to Death
5163	M	6-22-39	6-23	-	213	-	20	4.2	4
5167	M	6-22	6-23	6-28	249	-	20	4.9	10
5168	M	6-22	6-23	-	266	-	20	5.3	3
5169	M	6-22	6-23	-	228	-	20	4.6	3
5160	F	6-22	6-23	-	244	-	20	4.8	4
5164	F	6-22	6-23	6-28	254	-	20	5.0	5
5165	F	6-22	6-23	6-28	234	-	20	4.6	14
5166	M	6-22	6-23	6-28	224	+ 60	20	4.4	-
5161	F	6-22	6-23	6-28	270	+ 16	20	5.4	-
5162	F	6-22	6-23	6-28	278	+ 2	20	5.6	-
4929	M	5-18	5-19	-	236	-	10	2.4	4
5033	M	6-1	6-2	6-6	225	-	10	2.2	5
5-37	M	6-1	6-2	6-6	270	-	10	2.7	10
5038	F	6-1	6-2	6-6	244	-	10	2.4	11
4927	M	5-18	5-19	5-23	222	+ 31	10	2.2	-
4930	M	5-18	5-19	5-23	276	+ 11	10	2.8	-
5035	M	6-1	6-2	6-6	266	+ 31	10	2.6	-
5036	M	6-1	6-2	6-6	238	0	10	2.4	-
4928	F	5-18	5-19	5-23	265	+ 9	10	2.6	-
5034	F	6-1	6-2	6-6	267	+ 23	10	2.6	-
4935	M	5-18	5-19	-	232	-	5	1.2	4
4938	M	5-18	5-19	5-23	263	-	5	1.3	5
4934	F	5-18	5-19	5-23	242	-	5	1.2	6
4936	F	5-18	5-19	-	252	-	5	1.3	3
4937	F	5-18	5-19	5-23	254	-	5	1.3	12
4939	F	5-18	5-19	-	223	-	5	1.1	3
4931	M	5-18	5-19	5-23	240	+ 18	5	1.2	-
4932	M	5-18	5-19	5-23	272	+ 25	5	1.4	-
4933	F	5-18	5-19	5-23	265	+ 24	5	1.3	-
4940	F	5-18	5-19	5-23	230	+ 9	5	1.2	-

Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12443A

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 Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 pages 1, 2 pages _____

Notes:

Contractor reviewer: JW Date: 1/17/96

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:

Submission # BEHQ-0992-12443 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Union Carbide Corporation

SUB. DATE: 09/24/92 OTS DATE: 09/29/92 CSRAD DATE: 05/01/95

CHEMICAL NAME:

Carbitol, butyl

CASE# 112-34-5

INFORMATION REQUESTED: FLWP DATE: _____
 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TECH)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)
 DISPOSITION:
 0639 REFER TO CHEMICAL SCREENING
 0678 CAP NOTICE

VOLUNTARY ACTIONS:
 0401 NO ACTION REPORTED
 0402 STUDIES PLANNED/IN PROGRESS
 0403 NOTIFICATION OF WORKER HEALTH
 0404 LABEL/MSDS CHANGES
 0405 PROCESS/HANDLING CHANGES
 0406 APP/USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLIN	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 CHEM/PHYS 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. OCCUR/REL/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 MSDS	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	0239 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAGE DATA: NON-CBI INVENTORY ONGOING REVIEW SPECIES TOXICOLOGICAL CONCERN: USE: PRODUCTION:
YES YES (DROP/REFER) RBT LOW
NO NO (CONTINUE) GP MED
IN TERMINI REFER RAT HIGH

COMMENTS

12443A

L

Butyl carbitol: Acute oral toxicity in rats, guinea pigs, and rabbits is of low concern. Single oral gavage doses to male rats (4-10/dose) at levels of 3,000, 5,000, 6,000, 8,000, and 10,000 mg/kg were lethal (0/4, 2/10, 6/10, 5/10, and 4/4, respectively). The LD₅₀ was 6,500 mg/kg in rats. Single oral gavage doses to guinea pigs (2-10/dose) at levels of 1,000, 1,200, 1,500, 1,800, 2,000, 2,500, 3,000, 4,000, 5,000, 6,000, and 8,000 mg/kg were lethal (0/3, 0/3, 2/10, 1/10, 7/10, 8/10, 2/2, 2/2, 2/2, 4/4, and 4/4, respectively). The LD₅₀ was 2,000 mg/kg in guinea pigs. Single oral gavage doses to rabbits (6-10/dose) at levels of 1,500, 2,000, 2,500, 3,000, and 4,000 mg/kg were lethal (0/6, 2/10, 2/10, 7/10, and 6/6, respectively). The LD₅₀ was 2,500 mg/kg in rabbits.

L

Butyl carbitol: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (5-10/dose) at levels of 100, 250, 500, 1,000, 2,000, and 4,000 mg/kg (converted from mL/kg assuming density is 1) were lethal (1/6, 1/6, 2/8, 2/8, 5/10, and 5/5, respectively). There were no significant clinical signs or gross pathological effects.

L

Butyl carbitol acetate: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (4-10/dose) at levels of 6,000, 8,000, 10,000, 20,000, 40,000, and 50,000 mg/kg were lethal (0/4, 3/10, 3/10, 5/10, 5/10, and 5/10, respectively). The LD₅₀ was 20,000-50,000 mg/kg.

L

Carbitol acetate: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (4-12/dose) at levels of 5,000, 10,000, 15,000, 20,000, and 30,000 mg/kg were lethal (2/10, 4/12, 1/8, 1/4, and 4/10, respectively).

L

Cellosolve acetate: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (4-10/dose) at levels of 15,000, 20,000, and 50,000 mg/kg were lethal (0/4, 6/10, and 4/4, respectively). The LD₅₀ was approximately 20,000 mg/kg.

L

Methyl carbitol: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (4-10/dose) at levels of 1,000, 3,000, 5,000, 10,000, 20,000, and 30,000 mg/kg were lethal (3/8, 1/4, 6/10, 4/10, 7/10, and 4/4, respectively). The LD₅₀ was 8,000 mg/kg.

L

Methyl cellosolve acetate: Acute dermal toxicity in guinea pigs is of low concern. Single dermal doses to guinea pigs (4-10/dose) at levels of 5,000, 10,000, 15,000, and 20,000 mg/kg were lethal (3/10, 6/10, 4/10, and 4/4, respectively). The LD₅₀ was 10,000 mg/kg.