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September 24, 1992

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U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

8EHQ-92-12446

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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 reports pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). These reports describe acute toxicity studies with diethylene glycol monobutyl ether (CASRN 112-34-5).

- (1) "Toxicity Studies With Diethylene Glycol Monobutyl Ether: I. Acute Oral LD₅₀ Eastman Kodak Co., April 1, 1984.
- (2) "Toxicity Studies With Diethylene Glycol Monobutyl Ether: III. Six Weeks Repeated Dose Study", April 1, 1984.

Complete summaries of these reports are attached.

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

(None)

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

monobut

mm
9/1/92

②

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 reports the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of these reports. 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 G. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summaries, and reports)

SUMMARY

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER

I. ACUTE ORAL LD₅₀

Eastman Kodak Company

April, 1984

1.

SUMMARY

2.

Results and Discussion

Acute oral LD₅₀ values for DB in fasted male rats and mice and fed male rats and mice are presented in Table 1. These results are in agreement with reports in the literature which indicate that the mono ethers of diethylene glycol have a low degree of acute oral toxicity.⁽¹⁾

In both species, DB was less toxic in the fed animals, and was more toxic for mice than for rats in both fasted and fed animals.

Clinical signs of toxicity for both fed and fasted animals of both species were inactivity, labored breathing, rapid respiration, anorexia, slight to moderate weakness, tremors, prostration and death. Deaths occurred from within one to four days following treatment. Hematuria was not observed at any dose level of DB in either species.

No compound-related effects were observed on gross autopsy.

SUMMARY

3.

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER
III. SIX WEEKS REPEATED DOSE STUDY

Eastman Kodak Company

April, 1984

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SUMMARY

4.

Conclusions

No spontaneous deaths were observed in any of the dose groups. Two animals receiving the high dose were euthanized because of their moribund condition.

A statistically significant depression in body weight (22%) and food consumption (20%) was observed for animals receiving the high dose. For the low and intermediate dose groups, body weight and food consumption were not significantly different from those of the control animals.

Significant compound related histopathology was found in the spleens of DB treated rats. This consisted primarily of splenic congestion in 6/10 rats at the high dose only. Red pulp hypocellularity, hemosiderin and extramedullary hematopoiesis were also present in some animals at the high dose.

Kidney effects included proteinaceous casts in the proximal convoluted tubules. Hyaline droplet degeneration was seen in all test groups and in all control animals and was not considered to be treatment related.

No effects were seen on absolute testes weight or on testicular histopathology. Organ weight effects included increased absolute and relative liver and spleen weights at the high and intermediate doses.

SUMMARY

5.

Hematologically, significant decreases in red cells and hemoglobin were seen after treatment with DB, but only at the high dose level. No effects on clinical chemistry were noted.

For Distribution by CMA
SPECIAL NEEDS

From Lori Hamon
Ref. No. B-E-T-70-111
Date 5-17-84

B-15

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER

I. ACUTE ORAL LD₅₀

Eastman Kodak Company

April, ¹/₁ 1984

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER

I. ACUTE ORAL LD₅₀

Introduction

Available data indicate that the glycol ethers, in general, have a low to moderate degree of toxicity. The majority of these compounds are only slightly irritating to the skin, though most are readily absorbed percutaneously. Eye contact produces moderate irritation. Prolonged or repeated inhalation of the vapors may cause irritation and adverse systemic effects; however, the relatively low volatility of these ethers should prevent exposure to toxic concentrations at normal temperatures.⁽¹⁾

Several toxicity studies were designed in our laboratory to specifically study the toxicity of diethylene glycol monobutyl ether (DB). This report describes the results of acute oral LD₅₀ studies in rats and mice.

Materials and Methods

The test compound was supplied by the Texas Eastman Company. An aliquot of each test sample was submitted to the Kodak Park Industrial Laboratory for identification of contaminants. Gas

chromatographic analyses showed that the test compound was > 99.5% pure. The chemical structure of DB was confirmed by infrared spectroscopy.

The test species were Charles River COBS, CD, BR male rats (150-200 g) and Charles River, COBS, CD-1 male mice (15-17 g). The animals of both species were received from the same supplier at the same time. All animals were quarantined and acclimated in our laboratory prior to being randomly assigned to the study. Two batches of both species were received approximately two months apart. The acute oral LD₅₀ was determined in fasted and fed animals, with a period of two months between experiments. Each series of LD₅₀ determinations (fasted and fed) in both species were conducted exactly the same except for the fasting prior to dosing and the batch of animals used.

Twenty-five animals of each species were divided into five dose groups of five rats or mice each. The doses given were calculated on a mM/kg basis for the purpose of comparison with other compounds and ranged from 10.5 to 168 mM/kg progressing by a factor of two. Dose administration was by gavage, undiluted, using a glass syringe fitted with a polypropylene catheter. The animals were individually housed in suspended wire-bottom cages. Water was available ad libitum and except for the removal of the food from the fasted animals 16-20 hours prior to treatment, food was available ad libitum.

General appearance and activity, pharmacologic and toxicologic signs and mortality were checked twice daily except on weekends and holidays. The appearance of stools and urine on the trays was noted and individual body weights were done prior to dosing and at the end of the two week observation period.

Animals that died during the study and all survivors were necropsied and examined for gross pathology. The survivors within a particular compound group were necropsied by the same prosector beginning with the high dosed animals and proceeding to the low dosed groups. The LD₅₀ with its 95% confidence interval was calculated using the method of Thompson and Weil. (2)

Results and Discussion

Acute oral LD₅₀ values for DB in fasted male rats and mice and fed male rats and mice are presented in Table 1. These results are in agreement with reports in the literature which indicate that the mono ethers of diethylene glycol have a low degree of acute oral toxicity. (1)

In both species, DB was less toxic in the fed animals, and was more toxic for mice than for rats in both fasted and fed animals.

Clinical signs of toxicity for both fed and fasted animals of both species were inactivity, labored breathing, rapid respiration, anorexia, slight to moderate weakness, tremors, prostration and death. Deaths occurred from within one to four days following treatment. Hematuria was not observed at any dose level of DB in either species.

No compound-related effects were observed on gross autopsy.

References

1. Rowe, V. K., Derivatives of Glycols, Chapter XXXVI in Industrial Hygiene and Toxicology, Vol. II, 2nd Edition, F. A. Patty, Ed., pp. 1537-1592, Interscience Publishers, Inc., 1963.
2. Thompson, W. R. and Weil, C. S., On the Construction of Tables for Moving Average Interpolation. Biometrics 8:51-54, 1952.

Table 1. Acute Oral LD₅₀'s of Diethylene Glycol Monobutyl Ether in Fasted and Fed Rats and Mice

Animal	LD ₅₀ (mmol/kg)	LD ₅₀ (mg/kg)
Rat (fasted)	45.0 (32.1 - 63.2) ^a	7292 (5200 - 10238)
Rat (fed)	59.4 (40.1 - 87.9)	9623 (6496 - 14240)
Mouse (fasted)	14.9 (9.1 - 24.2)	2406 (1474 - 3920)
Mouse (fed)	34.1 (22.0 - 52.9)	5526 (3564 - 8570)

^a 95% confidence interval

AFDK
Red Blood Cell
Destruction
Hyaline Drop let
Nephropathy

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER

III. SIX WEEKS REPEATED DOSE STUDY

Eastman Kodak Company

April, 1984

TOXICITY STUDIES WITH DIETHYLENE GLYCOL MONOBUTYL ETHER

III. SIX WEEKS REPEATED DOSE STUDY

Introduction

The ethers of ethylene and diethylene glycol have been extensively used in industry for the past 15 to 40 years. Available data indicate that the glycol ethers, in general, have a low to moderate degree of toxicity. The majority of these compounds are only slightly irritating to the skin, though most are readily absorbed percutaneously. Eye contact produces moderate irritation. Prolonged or repeated inhalation of the vapors may cause irritation and adverse systemic effects; however, the relatively low volatility of these ethers should prevent exposure to toxic concentrations at normal temperatures.⁽¹⁾

Several studies were designed in our laboratory to specifically investigate the toxicity of diethylene glycol monobutyl ether (DB). This report describes the results of a six week repeated dose (gavage) study in male rats.

Materials and Methods

The test compound was supplied by the Texas Eastman Company. An aliquot of each test sample was submitted to the Kodak Park

Industrial Laboratory to be analyzed for purity and verification of molecular structure. Gas chromatographic results showed that DB was > 99.5% pure. The molecular structure of the compound was confirmed by infrared spectroscopy.

Male, albino rats (CR, COBS*, CD, BR) with an average body weight of 235.7 ± 15.1 grams purchased from the Charles Rivers Breeding Laboratories at Wilmington, MA, were used in the study. The animals were quarantined and acclimated to our laboratory for two weeks prior to the start of the study. The treatment group consisted of 30 rats and the control group of 10 rats. The treatment group was further subdivided into three dose groups of 10 rats each.

Doses of 3564, 1782 or 891 mg of DB per kilogram of body weight equivalent to 1/2, 1/4 or 1/8 the acute oral (fasted) LD₅₀ determined in our laboratory were administered undiluted by gavage, five days per week for six weeks. This schedule provided 29-33 doses over a 44 day period. The control animals were handled similarly to the treated rats except that they received a volume of distilled water, equal to the largest volume given a treated animal. All doses were recalculated weekly to adjust for changes in body weights.

The animals were housed individually in suspended wire cages and Purina Rodent Chow 5001* and water, via an automatic watering system, were available ad libitum.

Individual body weights were recorded on days 0, 3, 6, 13, 20, 27, 34 and 41 of the study. Individual animal feed consumption data were recorded at the time the animals were weighed.

Animals were observed daily, except on weekends, for clinical signs of systemic toxicity and for deviations from normal with respect to general appearance and behavior. The appearance of urine and feces on the dropping trays was noted. Mortality was checked daily.

Blood was drawn from the inferior vena cava just prior to autopsy for hematologic and serum clinical chemistry determinations. These determinations consisted of hemoglobin concentration, hematocrit, red blood cell counts, red cell indices, total and relative white cell counts, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, lactic dehydrogenase, urea nitrogen, creatinine and glucose.

Animals that died spontaneously were autopsied as soon as possible and moribund animals were euthanized with CO₂ and autopsied.

Tissues were collected for histopathologic examination.

At termination, the survivors were killed by CO₂ inhalation and the following tissues were collected, fixed in 10% buffered formalin, processed by standard histologic techniques and examined by light microscopy: lung, heart, thymus, kidneys, liver, spleen, brain, salivary glands, stomach, cecum, colon, duodenum, jejunum,

ileum, pancreas, esophagus, adrenal glands, pituitary, thyroid, parathyroid, trachea, mesenteric lymph nodes, testes, epididymides, prostate, seminal vesicles, coagulating gland, bone marrow, tongue and nasal cavities. Eyes were fixed in Zenker's solution. Prior to being sectioned for fixation the liver, kidneys, heart, testes, brain and spleen were carefully trimmed and weighed for organ/body weight comparisons.

Results and Discussion

Mortality

The disposition of all animals on the study is shown in Table 1. No significant compound related mortality occurred in any dose group.

Body Weight and Feed Consumption

Individual body weights and feed consumption data with means and standard deviations, are listed in Tables 2 and 3. These data are presented graphically in Figures 1 and 2. Only the high dose of DB produced significant reductions in body weight gain and feed consumption. The intermediate and lower doses of DB produced slight, statistically non-significant, reductions in mean body weight gain.

Hematology and Clinical Chemistries

The individual values of the hematologic and serum clinical chemistry determinations are presented in Tables 4 and 5, respectively. The major hematologic effects produced by the test compound were effects on the red blood cells.

Diethylene glycol monobutyl ether (DB) decreased hemoglobin concentration and total red cells at the high and intermediate dose levels. Calculated red cell indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), reflected abnormal red cell morphology (microcytosis, macrocytosis, hypochromasia). The high and intermediate doses of DB increased MCV and MCH and decreased the MCHC.

The high and intermediate doses of DB produced significant decreases in the glucose level. This change, though statistically significant, was only slightly different compared to the controls and its toxicologic significance is uncertain.

Organ/Body Weight Comparisons

The individual terminal body and organ weights are presented in Table 6.

Significant reductions in mean terminal body weights were seen at all dose levels of DB.

Absolute and relative spleen weights of the animals given the high and intermediate doses of DB were significantly increased. The high and intermediate doses of DB significantly increased the absolute and relative weight of the liver.

Other organ weight changes noted were a reflection of the decreased body weight gain seen in these groups.

Clinical Signs

The high dose of diethylene glycol monobutyl ether (DB) produced bloody urine and blood around the nose and mouth in one rat after 23 days on the study. Other clinical signs noted at this dose level were dyspnea, prostration, and unkempt hair coat. No clinical signs of toxicity were seen at the intermediate and low dose levels.

Gross and Histopathology

Blood was seen in the urinary bladder of some animals from the high dose group of DB that died prior to termination and dark, enlarged spleens were seen in some of the survivors. No abnormalities were noted in the intermediate and low dose animals of DB.

Histopathologic lesions are listed in Table 7. All doses of DB produced hyperkeratosis of the stomach and acanthosis of the stomach was seen in a few animals.

Splenic congestion and red pulp hypocellularity and hemosiderin-like pigmentation were seen at the high dose of DB.

Histologically, renal effects included hyaline droplet degeneration, proteinaceous casts, and hemosiderin in the proximal convoluted tubules. The proteinaceous casts and hemosiderin appeared to be compound related but may have been secondary to the hematologic effects. The hyaline droplet degeneration was also seen in all ten control rats. Thus, the significance of this finding is uncertain.

Conclusions

No spontaneous deaths were observed in any of the dose groups. Two animals receiving the high dose were euthanized because of their moribund condition.

A statistically significant depression in body weight (22%) and food consumption (20%) was observed for animals receiving the high dose. For the low and intermediate dose groups, body weight and food consumption were not significantly different from those of the control animals.

Significant compound related histopathology was found in the spleens of DB treated rats. This consisted primarily of splenic congestion in 6/10 rats at the high dose only. Red pulp hypocellularity, hemosiderin and extramedullary hematopoiesis were also present in some animals at the high dose.

Kidney effects included proteinaceous casts in the proximal convoluted tubules. Hyaline droplet degeneration was seen in all test groups and in all control animals and was not considered to be treatment related.

No effects were seen on absolute testes weight or on testicular histopathology. Organ weight effects included increased absolute and relative liver and spleen weights at the high and intermediate doses.

Hematologically, significant decreases in red cells and hemoglobin were seen after treatment with DB, but only at the high dose level. No effects on clinical chemistry were noted.

References

1. Rowe, V. K., Derivatives of Glycols, in "Industrial Hygiene and Toxicology, Chapter XXXVI, Vol. II, 2nd Edition, F. A. Patty, Ed., pp. 1537-1592, Interscience Publishers, Inc., 1963.

Table 1. Repeated Dose Study with Diethylene Glycol
Monobutyl Ether in Rats - Disposition of Animals

Dose in mg/kg (mmol/kg)	Spontaneous Deaths	Moribund Sacrifice	Intubation Error	Killed at Term
3564(22)	0	2	4	4
1782(11)	0	0	2	8
891(5.5)	0	0	1	9
Control ^a	0	0	0	10

^a Received a volume of distilled water equal to the highest volume given to a treatment group.

Table 2. Body Weights (g)

BODY WEIGHT		DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 22 MMOL/KG							
RAT	DAY 0	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41	
181	237	221	248	290	275	321	330	335	
182	229	226	234						
183	221	205	234	263	254	276	292	299	
184	257	228	253	310	311				
185	240								
186	214	199	207	262	255				
187	241	246	181	259					
188	217	199	215	265	262	293	289	292	
189	224	210	244	287	290	326	337	338	
190	231								
AVG	231.1	216.8*	229.8*	276.6*	274.8*	304.0 ¹	312.0*	316.0*	
S. D.	13.0	16.5	26.4	19.3	22.1	23.7	25.0	23.9	

BODY WEIGHT		DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 11 MMOL/KG							
RAT	DAY 0	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41	
191	262	275	283	322	322	349	372	395	
192	221	246	265	306	333	365	386	392	
193	252								
194	245	256	278						
195	242	259	276	312	323	356	366	386	
196	258	271	288	329	343	369	387	414	
197	216	226	244	277	291	316	337	356	
198	221	223	244	267	281	304	329	349	
199	217	229	249	277	293	325	344	366	
200	234	254	276	305	324	361	370	383	
AVG	236.8	248.8	267.0	299.4	313.8	343.1	361.4	380.1	
S. D.	17.5	19.2	17.2	22.9	22.4	24.7	22.1	21.7	

BODY WEIGHT		DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 5.5 MMOL/KG							
RAT	DAY 0	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41	
201	239								
202	230	244	260	300	319	346	370	380	
203	228	236	255	290	306	343	357	374	
204	206	219	237	260	266	288	306	320	
205	241	257	277	317	322	361	381	401	
206	235	246	264	296	307	340	353	371	
207	235	256	273	307	316	348	369	383	
208	240	263	282	321	336	378	402	421	
209	218	234	251	284	290	322	342	351	
210	221	235	254	293	311	341	353	371	
AVG	229.3	243.3	261.4	296.4	308.1	340.8	359.2	374.7	
S. D.	11.3	13.9	14.2	18.3	20.2	25.0	26.8	28.5	

*Statistically significant $p \leq 0.05$

Table 2 (cont.). Body Weights (g)

BODY WEIGHT		CONTROLS							
RAT	DAY 0	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41	
271	226	236	261	280	304	339	363	374	
272	247	259	280	330	358	391	427	449	
273	211	230	256	290	311	342	356	381	
274	257	269	273	329	342	375	406	410	
275	207	218	234	266	271	303	316	330	
276	241	272	288	328	341	379	406	424	
277	252	266	276	307	330	363	379	400	
278	234	259	277	322	345	372	397	414	
279	248	276	292	350	372	416	440	456	
280	223	248	263	304	316	353	383	402	
AVG	234.6	253.3	272.0	311.4	328.8	363.3	387.3	405.0	
S D	17.3	19.6	18.6	25.1	29.1	31.3	36.3	38.5	

Table 3. Feed Consumption (g/rat/day)

FEED CONSUMPTION DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 22 MMOL/KG							
RAT	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41
181	10.7	16.2	20.5	19.0	20.8	20.4	20.5
182	12.0	17.3					
183	9.0	15.0	18.8	18.1	18.0	18.5	18.6
184	10.0	15.0					
185							
186	8.7	10.8	17.0	18.1	18.6		
187	14.7	8.7	15.1				
188	7.0	12.0	18.1	17.6	18.3	18.5	18.4
189	11.7	17.0	21.0	20.3	20.8	20.8	20.4
190							
AVG	10.47*	14.00*	19.15*	18.90*	19.30*	19.55*	19.47*
S D	2.37	3.14	2.11	1.17	1.39	1.22	1.13

FEED CONSUMPTION DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 11 MMOL/KG							
RAT	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41
191	20.7	21.7	23.8	22.8	22.8	23.6	24.0
192	23.3	24.0	25.5	25.5	26.2	26.8	27.2
193							
194	16.3	17.2					
195	17.3	20.2	20.2	22.0	22.6	22.3	23.0
196	21.0	22.2	23.0	23.7	23.2	23.9	24.4
197	16.7	18.7	19.5	20.2	20.7	21.6	22.0
198	16.0	24.0	22.3	21.3	21.8	22.4	22.7
199	17.7	18.8	20.2	20.9	21.1	21.7	22.6
200	21.0	21.8	22.5	22.7	23.2	22.6	23.1
AVG	18.04*	21.16	22.47	22.45	22.70	23.11	23.65
S D	2.63	2.07	1.64	1.65	1.70	1.70	1.62

FEED CONSUMPTION DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 5.5 MMOL/KG							
RAT	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41
201							
202	20.0	20.0	22.4	22.4	23.0	23.4	23.6
203	19.7	21.5	22.8	22.7	23.1	23.3	23.5
204	21.7	20.5	21.5	20.8	20.6	20.9	21.1
205	21.7	23.3	24.7	24.1	24.4	24.4	24.9
206	22.0	22.5	23.5	22.7	22.9	22.9	23.2
207	22.3	23.2	24.0	23.0	23.5	23.9	23.9
208	21.7	23.3	23.5	24.0	22.7	22.8	22.7
209	20.7	20.3	21.5	21.3	21.6	21.9	22.1
210	20.7	20.7	21.7	21.8	23.0	23.0	23.3
AVG	21.17	21.73	22.7	22.62	23.20	23.37	23.59
S D	0.92	1.36	1.26	1.13	1.71	1.60	1.59

*Statistically significant from controls $p \leq 0.05$

Table 3 (cont.). Feed Consumption (g/rat/day)

FEED CONSUMPTION		CONTROLS					
RAT	DAY 3	DAY 6	DAY 13	DAY 20	DAY 27	DAY 34	DAY 41
271	20.7	22.0	17.9	19.4	20.6	21.4	22.1
272	21.3	23.2	20.2	25.3	25.8	26.3	26.7
273	18.0	18.8	21.2	21.9	22.4	23.2	23.7
274	24.0	25.2	25.3	24.6	25.0	25.1	24.7
275	21.3	20.0	20.6	20.0	20.3	20.4	20.5
276	23.7	22.8	21.6	24.0	23.4	24.2	24.4
277	22.3	22.3	22.9	22.5	23.2	23.2	23.4
278	21.3	21.3	21.0	22.0	22.4	23.2	23.6
279	24.7	25.2	27.1	27.1	27.6	27.9	28.1
280	22.0	21.8	22.7	22.8	23.1	23.4	23.7
AVG	21.93	22.26	22.53	22.76	23.43	23.83	24.09
S D.	1.93	2.02	2.78	2.36	2.26	2.20	2.14

Table 4. Hematology

HEMATOLOGY														
DIETHYLENE GLYCOL MONOBUTYL ETHER (DB1) 22 MMOL/KG														
RAT	HB	C.V.	RBC	MCV	MCH	MCHC	MBC	POLY	LYMPH	EOS	MONO	BAZO	BAWD	
181	11.9	50	5.96	81.9	20.0	23.8	12900	20	75	2	3	0	0	
183	12.7	51	6.23	81.9	20.4	24.9	12200	25	69	0	6	0	0	
188	13.5	46	6.87	67.0	19.7	29.3	9700	11	88	0	0	0	0	
189	12.7	43	7.49	57.4	17.0	29.5	9600	14	74	4	4	0	0	
192	12.8	50	7.81	64.0	17.7	27.4	10400	14	82	0	4	0	0	
196	11.9	39	6.94	56.2	17.1	30.5	6900	16	82	0	2	0	0	
197	13.4	46	7.47	61.6	17.9	29.1	8300	12	86	0	2	0	0	
198	13.2	48	7.67	62.6	17.2	27.5	11500	24	71	1	3	0	0	
AVO	13.26*	46.4	7.569*	61.12*	17.52	28.75*	10950.0	13.5	79.9	0.8	3.3	0.0	0.0	0.3
B.D.	0.69	5.0	0.329	4.17	0.39	2.02	3206.2	3.7	5.2	1.4	1.9	0.0	0.0	0.5
HEMATOLOGY														
DIETHYLENE GLYCOL MONOBUTYL ETHER (DB1) 5.9 MMOL/KG														
RAT	HB	C.V.	RBC	MCV	MCH	MCHC	MBC	POLY	LYMPH	EOS	MONO	BAZO	BAWD	
202	13.9	45	8.46	53.2	16.4	30.9	11200	21	74	2	3	0	0	
203	15.2	51	8.89	57.4	17.1	29.8	14000	20	76	0	4	0	0	
204	14.2	46	8.62	51.4	16.5	30.9	9400	4	93	0	4	0	0	
205	14.7	49	8.25	57.4	17.8	30.0	8500	26	67	1	6	0	0	
206	14.1	44	8.41	52.3	16.8	32.0	7700	18	73	3	6	0	0	
207	14.2	45	8.10	53.6	17.9	32.2	15400	9	91	0	0	0	0	
208	14.2	45	8.20	54.9	17.3	31.6	13700	11	87	1	1	0	0	
209	14.9	47	8.65	54.1	17.2	31.7	14600	4	95	1	0	0	0	
210	13.8	44	8.13	54.1	17.0	31.4	10600	16	83	0	1	0	0	
AVO	14.39	46.2	8.413	54.96	17.11	31.17	11677.8	14.3	82.1	0.9	2.8	0.0	0.0	0.0
B.D.	0.47	2.4	0.269	2.23	0.52	0.84	2036.7	7.8	10.0	1.1	2.4	0.0	0.0	0.0

*Statistically significant compared to controls p 50,05

Table 4 (cont.). Hematology

HEMATOLOGY		CELLS											
RAI	HR	C.V.	RBC	MCV	MCH	MCHC	MRC	POLY	LYMPH	EOS	MONO	PLAS	BAND
271	13.0	47	9.34	49.3	13.7	31.9	12700	12	81	0	7	0	0
272	14.4	46	8.09	56.9	17.8	31.3	11500	18	79	0	3	0	0
273	14.8	46	8.91	51.4	16.6	32.2	7900	17	88	0	0	0	0
274	14.1	45	8.46	50.2	16.7	31.3	8400	21	73	1	5	0	0
275	13.4	48	8.77	51.7	17.6	32.1	9400	13	81	1	3	0	0
276	13.7	48	9.38	59.1	16.4	32.7	10500	10	90	0	0	0	0
277	14.4	43	8.72	51.7	16.4	32.0	8700	19	76	3	2	0	0
278	13.4	49	8.89	59.1	17.3	31.4	9400	14	78	1	7	0	0
279	14.9	47	8.46	50.6	17.6	31.7	12400	14	78	1	3	0	0
280	14.5	48	8.25	50.2	17.6	30.2	8400	19	77	1	3	0	0
AVG	14.86	46.9	8.771	53.69	16.97	31.68	10030.0	15.6	80.3	0.8	3.3	0.0	0.0
S.D.	0.52	1.4	0.497	2.98	0.70	0.68	1923.0	3.8	5.5	1.0	2.4	0.0	0.0

Table 5. Clinical Chemistries

CLINICAL CHEMISTRY DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 22 MMOL/KG

RAT	SGOT	SGPT	LDH	ALK PHOS	BUN	GLUC	CREATININE
181	88	76		244	12	87	0.50
183	85		424	184	19	86	0.55
188	65	29		278	17	97	0.50
189	95	37	681	171	11	128	0.50
AVG	78.3	32.7	652.5	219.3	14.8	98.5 [#]	0.512
S.D.	14.2	6.7	323.1	50.4	3.9	20.6	0.025

CLINICAL CHEMISTRY DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 11 MMOL/KG

RAT	SGOT	SGPT	LDH	ALK PHOS	BUN	GLUC	CREATININE
191	73	23	719	78	9	125	0.45
192	80	35	387	162	16	92	0.60
195	55	23	709	265	14	95	0.50
196	68	30	418	188	10	93	0.40
197	75	35	307	171	12	94	0.60
198	71	26	472	257	12	98	0.40
199	72	29	545		11	102	0.40
200	91	37	314	193	13	102	0.50
AVG	78.1	30.1	493.9	187.7	12.1	110.1 [#]	0.481
S.D.	9.9	6.0	151.7	63.0	2.2	31.0	0.084

CLINICAL CHEMISTRY DIETHYLENE GLYCOL MONOBUTYL ETHER (DB) 5.5 MMOL/KG

RAT	SGOT	SGPT	LDH	ALK PHOS	BUN	GLUC	CREATININE
202	78	25	632	309	13	144	0.50
203	116	33		190	14	102	0.60
204	77	27	314	149	10	121	0.50
205	65	23	269	163	16	129	0.60
206	84	17	420	141	14	132	0.55
207	75	13	322	174	13	107	0.50
208	67	24	300	185	11	126	0.50
209	67	28	455	190	13	175	0.50
210	69	37	322	232	12	134	0.50
AVG	77.6	25.2	392.0	192.6	12.9	132.4	0.528
S.D.	15.7	7.4	120.5	51.2	1.8	23.6	0.044

*Statistically significant compared to controls $p \leq 0.05$

Table 5 (cont.). Clinical Chemistries

CLINICAL CHEMISTRY		CONTROLS					
RAT	SCOT	SCPT	LDH	ALK PHOS	BUN	GLUC	CREATININE
271	74	32	303	116	10	132	0.50
272	93	23	272	164	12	148	0.55
273	91	19	1082	129	11	121	0.45
274	63	32	302	190	11	144	0.50
275	71	28	336	223	12	133	0.60
276	108	23	1152	248	15	143	0.60
277	81	41	304	203	12	137	0.50
278	68	18	282	206	10	140	0.50
279	90	36	897	143	11	152	0.50
280	61	17	350	151	9	166	0.55
AVG	80.2	26.9	549.8	177.3	11.3	141.8	0.525
S.D.	15.0	8.2	354.3	43.3	1.4	13.5	0.049

Table 6. Organ/Body Weights

ORGAN WT. X BODY WT DIETHYLENE GLYCOL MONOETHYL ETHER (DM) 22 MG/KG													
RAT	BODY	LIVER WT	%	TRIDY WT	%	HEART WT	%	TESTES WT	%	BRAIN WT	%	SPLEEN WT	%
181	302	14.76	4.87	2.05	1.01	1.04	0.34	3.18	1.05	2.04	0.68	1.22	0.40
182	261	10.27	3.93	2.11	0.82	0.95	0.36	2.62	1.00	1.78	0.68	1.36	0.52
188	261	12.20	4.67	2.42	0.73	1.23	0.47	2.42	0.93	1.79	0.69	1.46	0.56
189	304	13.71	4.51	2.72	0.89	0.93	0.31	2.79	0.92	1.91	0.63	1.04	0.34
AVG	282.0*	12.720*	4.493*	2.140	0.712*	1.037	0.370*	2.792	0.975*	1.880	0.670*	1.270*	0.459*
S.D.	24.3	1.930	0.404	0.373	0.079	0.137	0.070	0.323	0.061	0.122	0.027	0.182	0.102
ORGAN WT. X BODY WT DIETHYLENE GLYCOL MONOETHYL ETHER (DM) 11 MG/KG													
RAT	BODY	LIVER WT	%	KIDNEY WT	%	HEART WT	%	TESTES WT	%	BRAIN WT	%	SPLEEN WT	%
191	356	10.37	2.91	2.03	0.82	1.15	0.32	3.43	0.96	1.77	0.50	1.38	0.39
192	367	13.74	3.75	2.25	0.89	1.28	0.35	2.95	0.80	2.02	0.55	0.99	0.27
193	356	12.08	3.41	3.17	0.89	1.22	0.34	3.22	0.90	2.02	0.57	0.80	0.22
196	372	13.60	3.66	3.40	0.91	1.17	0.31	2.95	0.79	2.05	0.55	0.98	0.26
197	326	11.15	3.42	2.34	0.78	1.00	0.31	2.81	0.86	1.97	0.60	0.79	0.24
198	303	10.50	3.47	2.52	0.83	1.16	0.38	3.11	1.03	1.85	0.61	0.83	0.27
199	335	11.75	3.51	2.63	0.79	1.11	0.33	3.16	0.94	2.05	0.61	0.82	0.24
200	351	12.93	3.68	3.01	0.86	1.30	0.37	3.13	0.89	1.91	0.54	0.96	0.27
AVG	345.8*	12.117*	3.502*	2.959	0.854*	1.174	0.339	3.095	0.894*	1.956	0.566	0.944*	0.270*
S.D.	23.0	1.356	0.265	0.318	0.043	0.096	0.026	0.192	0.081	0.104	0.039	0.195	0.057
ORGAN WT. X BODY WT DIETHYLENE GLYCOL MONOETHYL ETHER (DM) 5.5 MG/KG													
RAT	BODY	LIVER WT	%	KIDNEY WT	%	HEART WT	%	TESTES WT	%	BRAIN WT	%	SPLEEN WT	%
202	353	11.20	3.17	3.21	0.91	1.21	0.34	3.11	0.88	2.13	0.60	0.75	0.21
203	341	10.89	3.19	2.36	0.75	1.30	0.38	3.16	0.93	1.92	0.56	0.92	0.27
204	296	8.80	2.97	2.13	0.72	0.91	0.31	2.66	0.90	1.95	0.64	0.84	0.22
205	370	13.07	3.53	2.97	0.80	1.19	0.31	3.20	0.86	1.96	0.53	0.64	0.17
206	344	10.75	3.13	2.69	0.78	1.40	0.41	3.08	0.90	2.05	0.60	0.57	0.17
207	356	9.53	2.68	2.41	0.71	1.00	0.28	2.09	0.81	2.09	0.59	0.71	0.20
208	389	12.74	3.28	2.20	0.57	1.48	0.38	3.19	0.82	2.15	0.55	0.79	0.20
209	325	11.53	3.55	2.92	0.90	1.18	0.36	2.99	0.92	1.88	0.58	0.68	0.21
210	351	11.27	3.21	2.93	0.83	1.15	0.33	3.39	0.97	1.93	0.56	0.75	0.21
AVG	347.1*	11.084	3.190*	2.761	0.862	1.198	0.344*	3.074	0.888*	2.012	0.581*	0.717	0.207
S.D.	26.2	1.374	0.274	0.302	0.071	0.180	0.042	0.209	0.032	0.096	0.038	0.102	0.030

*Statistically significant from controls p < 0.05

Table 6 (cont.). Organ/Body Weights

14

RAY	BODY	LIVER WT	%	KIDNEY WT	%	HEART WT	%	TESTES WT	%	BRAIN WT	%	SPLEEN WT	%
271	351.	10.37	2.93	1.69	0.77	1.07	0.30	2.97	0.85	1.94	0.55	0.71	0.20
272	417.	12.24	2.94	1.43	0.12	1.33	0.32	3.11	0.75	2.01	0.48	0.73	0.18
273	353.	7.90	2.00	2.75	0.78	1.08	0.31	3.19	0.90	2.02	0.57	0.66	0.19
274	381.	11.23	2.93	2.00	0.73	1.15	0.30	2.95	0.77	1.76	0.51	0.84	0.22
275	312.	7.66	2.45	1.98	0.64	0.80	0.26	2.90	0.93	1.09	0.61	0.52	0.17
276	394.	9.04	2.30	2.52	0.64	1.29	0.33	3.20	0.81	1.93	0.49	0.59	0.14
277	347.	10.25	2.75	2.92	0.90	1.09	0.30	3.10	0.84	1.94	0.53	0.66	0.18
278	386.	11.12	2.94	2.19	0.75	1.23	0.32	2.01	0.73	2.06	0.53	0.53	0.14
279	432.	12.63	2.92	3.44	0.90	1.26	0.29	3.37	0.78	2.19	0.51	0.92	0.21
280	377.	10.73	2.95	2.90	0.77	1.12	0.30	3.15	0.84	2.15	0.57	0.61	0.16
AVO	377.0	10.587	2.702	2.934	0.750	1.142	0.303	3.075	0.820	2.009	0.535	0.673	0.179
S.D.	34.3	1.392	0.179	0.418	0.063	0.152	0.019	0.167	0.064	0.099	0.040	0.132	0.027

Table 7. Histopathology

Lesions/Dose	Diethylene Glycol Monobutyl Ether			Control
	High	Inter.	Low	
Testes:				
Atrophy, seminiferous tubules	0/10	0/10	-	0/10
Epididymides:				
Degenerated spermatazoa	0/10	0/10	-	0/10
Hypospermia				0/10
Thymus:	0/9	0/10	-	0/10
Stomach:				
Hyperkeratosis	8/10	10/10	10/10	0/10
Acanthosis	1/10	0/10	2/10	0/10
Liver:				
Hepatocytomegally				0/10
Anisokaryosis				0/10
Lack of cytoplasmic basophilia				0/10
Spleen:				
Congestion	6/10	0/10	-	0/10
Red pulp hypocellularity	1/10	0/10	-	0/10
Hemosiderin	1/10	0/10	-	0/10
Kidneys:				
Proximal convoluted tubules, hyaline droplet degeneration	9/10	8/10	10/10	10/10
Proteinaceous casts	9/10	5/10	1/10	0/10
Hemosiderin	1/10	2/10	0/10	0/10

Figure 1

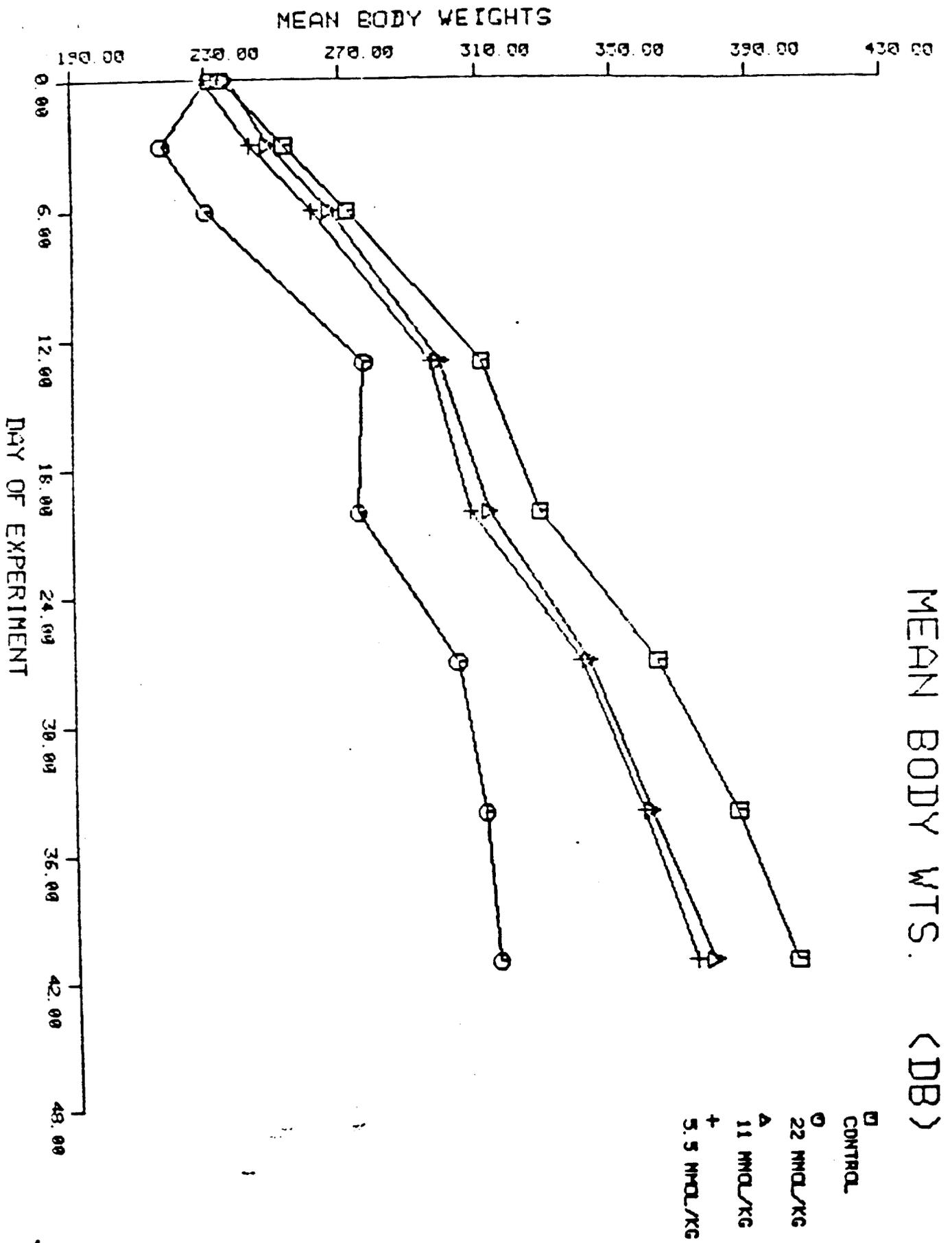
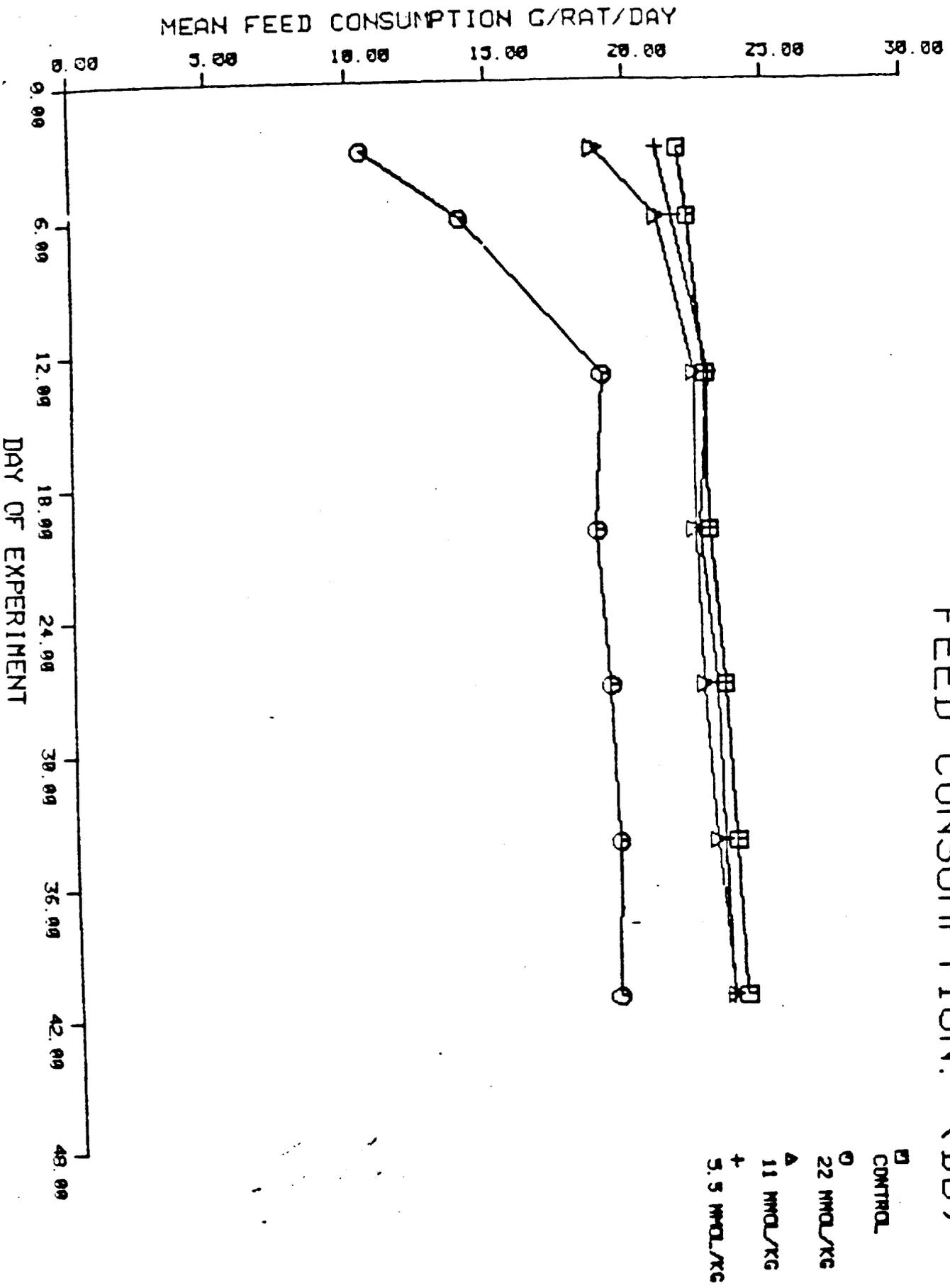


Figure 2

FEED CONSUMPTION. (DB)





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

MAY 08 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".

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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

12446A



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NON-CAP

CAP

Submission number: 12446 A

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

Notes:

Contractor reviewer : LPS

Date: 4/14/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:

Submission # BEHO-0992-12446 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Union Carbide Corporation

INFORMATION REQUESTED: FLWP DATE:

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

DISPOSITION:

- 0510 REFER TO CHEMICAL SCREENING
- 0511 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 (NI) ACTION REPORTED
- 0402 STUDY'S PLANNING/DATA REVIEW
- 0403 NOTIFICATION (H WINKER/KATHIEN)
- 0404 LABEL/MSDS (TIANCH)
- 0405 PROCESS/HANDLING (TIANCH)
- 0406 APPAUSE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 09/24/92 OTS DATE: 09/29/92 CSRAD DATE: 02/01/95

CHEMICAL NAME:

Diethylene glycol mono-butyl ether (DB)

CASE

112-34-5

INFORMATION TYPE:

P F C

0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
<u>0209</u>	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
<u>0212</u>	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
<u>0214</u>	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:

P F C

0216	EPICLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECOAQUA TOX	01 02 04
0221	ENV. OCCUREL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0229	METAB/PHARMACO (ANIMAL)	01 02 04
0230	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:

P F C

0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PRODUSE/PROC	01 02 04
0251	MSDS	01 02 04
0259	OTHER	01 02 04

TRIAJE DATA:

NON-CBI INVENTORY

ONGOING REVIEW

SPECIES

TOXICOLOGICAL CONCERN

USE:

PRODUCTION:

CAS SR

YES

NO

IN TRMIM

YES (DROP/REFER)

NO (CONTINUE)

REFER

RAT
MUS

LOW

MED

HIGH

LDSOs in rats
78400 mg/kg
in mice 73500 mg/kg

UNCLASSIFIED Rats were orally gavage with DB at 891, 1782 and 3564 mg/kg/day for 6 weeks. Treatment-related effects were seen in high dose level which included reduced body weights, hematological changes included decreased red cells & hemoglobin, splenic congestion characterized by pulp hypercellularity, hemosiderin and extramedullary hematopoiesis and kidney effects included proteinaceous cast in the proximal tubules.

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8EHQ-0992-12446 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Union Carbide Corporation

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 WORKERS/OTHERS
 0404 LABEL/MSDS CHANGES
 0405 PROCESS/HANDLING CHANGES
 0406 APP/USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

SUB. DATE: 09/24/92 OTS DATE: 09/29/92 CSRAD DATE: 02/01/95

CHEMICAL NAME: _____ CAS# 112-34-5

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. OCC/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
 YES
 CAS SR NO
 IN TERMINI

ONGOING REVIEW
 YES (DROP/REFER)
 NO (CONTINUE)
 REFER

SPECIES: RAT
MUS
TOXICOLOGICAL CONCERN:
LOW
 MED
 HIGH

USE: _____ PRODUCTION: _____

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Acute oral toxicity in rats and mice is of low concern based on LD₅₀ values of 7,292 mg/kg in fasted rats, 9,623 mg/kg in fed rats, 2,406 mg/kg in fasted mice, and 5,526 mg/kg in fed mice. Charles River Br male rats and CD-1 male mice (5/dose) received gavage doses between 10.5 to 168 mM/kg (doses not converted). Clinical signs for both species included inactivity, labored and rapid respiration, anorexia, weakness, tremors, and prostration. Hematuria was not observed at any dose in either species. No treatment-related effects were seen at necropsy.