



Contains NO CBI

1

UNION CARBIDE CORPORATION 38 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

A

September 24, 1992

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

8EHQ-92-12454

88920010642

INIT

Document Processing Center (TS-790)
Room L-100
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

OTS DOCUMENT RECEIPT
92 SEP 29 AM 10:03

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 a variety of toxicology data for ethylene glycol monomethyl ether (EGME; CASRN 109-86-4)

"Ethylene Glycol Monomethyl Ether (EGME)", TRT:ns, 5-20-82 (presumably a UCC document).

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)

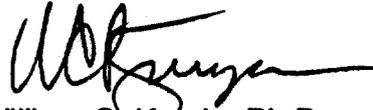
egme

6/2/95

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

Ethylene Glycol Monomethyl Ether - (EGME)

SUBCHRONIC

Nagano, et al, (1977, 1979)

Mice received 25 doses of EGME by gavage at levels of 2000, 1000, 500, 250, 125 or 62.5 mg/Kg.

Testicular atrophy, germinal cell epithelium damage, depressed red and white blood cell counts. ✓

No-effect level - 125 mg/Kg

Miller, et al, (1981)

Rats and mice exposed to EGME vapors at levels of 100, 300 or 1000 ppm for 9 days.

Testicular atrophy, depressed thymus gland weight, germinal cell epithelium damage, depressed bone marrow cellularity, depressed red and white blood cell counts. ✓

No-effect level - 100 ppm

Miller, et al, (1982)

Rats and rabbits exposed to EGME vapors at levels of 30, 100 and 300 ppm for 13 weeks.

Testicular atrophy, depressed thymus, germinal cell epithelium damage, depressed white and red blood cell counts. ✓

No-effect level - 100 ppm rats

Minimal-effect level - 30 ppm rabbits.

SUMMARY

2.

Ethylene Glycol Monomethyl Ether - EGME

Infertility in male rats with partial recovery 13 weeks after exposure. No effects on female reproductive performance. ✓

No-effect level (fertility): male rats - 100 ppm
female rats - 300 ppm.

TERATOLOGY

Nagano, et al, (1981)

Female mice received EGME at levels of 1000, 500, 250, 125, 62.5 and 31.25 mg/Kg by gavage on days 7 through 14 of gestation. ✓

Embryo and fetal toxicity, skeletal and gross anomalies, retarded development, white blood cell depression in mothers.

Minimal-effect level - 31.25 mg/Kg
(delayed ossification).

Miller, et al, (1982)

Female rabbits and rats were exposed to EGME at levels of 50, 10 and 3 ppm and mice were exposed to 50 and 10 ppm on days 6 through 15 (rabbits 6 through 18) of gestation.

An interim report indicated an increase in external and soft tissue malformations in rabbits. ✓

No-effect level: rabbits - 10 ppm
rats - 50 ppm
mice - 50 ppm

Skeletal evaluation should be completed by August.

Ethylene Glycol Monomethyl Ether - (EGME)

213-2-19
B-5

SUBCHRONIC

Nagano, et al, (1977, 1979)

Mice received 25 doses of EGME by gavage at levels of 2000, 1000, 500, 250, 125 or 62.5 mg/Kg.

Testicular atrophy, germinal cell epithelium damage, depressed red and white blood cell counts. ✓

No-effect level - 125 mg/Kg

Miller, et al, (1981)

Rats and mice exposed to EGME vapors at levels of 100, 300 or 1000 ppm for 9 days.

Testicular atrophy, depressed thymus gland weight, germinal cell epithelium damage, depressed bone marrow cellularity, depressed red and white blood cell counts. ✓

No-effect level - 100 ppm

Miller, et al, (1982)

Rats and rabbits exposed to EGME vapors at levels of 30, 100 and 300 ppm for 13 weeks.

Testicular atrophy, depressed thymus, germinal cell epithelium damage, depressed white and red blood cell counts. ✓

No-effect level - 100 ppm rats

Minimal-effect level - 30 ppm rabbits.

Miller, et al, (1982)
(CMA-Sponsored Study)

Male rabbits exposed to EGME vapors at levels of 30, 10 and 3 ppm for 13 weeks.

No observable adverse effects.

No-effect level - 30 ppm.

Rao, et al, (1982)
(Reproductive and Dominant
Lethal Study)

Rats exposed to EGME vapors at levels of 30, 100 and 300 ppm for 13 weeks.

Ethylene Glycol Monomethyl Ether - EGME

Infertility in male rats with partial recovery 13 weeks after exposure. No effects on female reproductive performance. ✓

No-effect level (fertility): male rats - 100 ppm
female rats - 300 ppm.

TERATOLOGY

Nagano, et al, (1981)

Female mice received EGME at levels of 1000, 500, 250, 125, 62.5 and 31.25 mg/Kg by gavage on days 7 through 14 of gestation. ✓

Embryo and fetal toxicity, skeletal and gross anomalies, retarded development, white blood cell depression in mothers.

Minimal-effect level - 31.25 mg/Kg
(delayed ossification).

Miller, et al, (1982)

Female rabbits and rats were exposed to EGME at levels of 50, 10 and 3 ppm and mice were exposed to 50 and 10 ppm on days 6 through 15 (rabbits 6 through 18) of gestation. ✓

An interim report indicated an increase in external and soft tissue malformations in rabbits. ✓

No-effect level: rabbits - 10 ppm
rats - 50 ppm
mice - 50 ppm

Skeletal evaluation should be completed by August.

MUTAGENICITY

McGregor, et al, (1981)
(Performed under contract with
NIOSH at Inveresk Research International)

Salmonella (Ames) test, 5 strains - negative for mutagenicity.

Unscheduled DNA Synthesis (UDS) negative for mutagenicity.

Cytogenetics (rat bone marrow) No indication of increased frequency of aberrations.

Dominant lethal study in rats. Results equivocal due to low pregnancy rates at highest level of exposure, 500 ppm.

Sperm abnormality test in mice. Abnormal sperm induced by EGME. ✓

Drosophila sex-linked recessive lethal test. Results equivocal.

Ethylene Glycol Monoethyl Ether - (EGEE)

SUBCHRONIC

Nagano, et al, (1977, 1979)

Mice received 25 doses of EGEE by gavage at levels of 4000, 2000, 1000 and 500 mg/Kg.

Testicular atrophy, germinal cell epithelium damage, decreased white blood cell count. ✓

No-effect level - 1000 mg/Kg

CMA-Sponsored Study
(Bio/Dynamics)

Rats and rabbits will be exposed to EGEE vapors for a 13-week period. Dosage levels of 25, 100 and 400 ppm.

Study to start by August, 1982.

TERATOLOGY

Hardin, B. D. (1981)
NIOSH Study conducted at
Battelle Pacific North-
West Laboratories

Rats and rabbits were exposed to EGEE vapors at levels of either 765 ppm or 200 ppm (rats) or 615 ppm or 160 ppm (rabbits) on days 1 through 19 (day 18 for rabbits) of gestation.

Complete resorptions of litters for both rats and rabbits at high level of exposure. Maternal toxicity in rabbits at both exposure levels; in rats at highest exposure level.

Embryo lethality in rabbits and fetotoxicity in both species at lower level of exposure. Increased soft tissue malformations and skeletal malformations in both species. ✓

No no-effect level established.

Nelson, B. K., et al, (1981)
NIOSH Study

* Rats exposed to EGEE vapors at level of 100 ppm at either days 7 to 13 or 14 to 20 of gestation. Behavioral tests conducted at days 10 through 80 of age.

A number of behavioral and neurochemical deviations noted. ✓
No no-effect level established.

Ethylene Glycol Monoethyl Ether - EGEE

CMA-Sponsored Study
ICI Central Toxicology Laboratory

Rats and rabbits exposed to EGEE vapors at levels of 10, 50 and 250 ppm (rats) and 10, 50 and 175 ppm (rabbits) on days 6 through 15 (rats) and 6 through 18 (rabbits) of gestation.

Preliminary results should be available in August, 1982. Final report in December, 1982.

MUTAGENICITY/CARCINOGENICITY

NIEHS (1982 Report)

Salmonella (Ames) test - negative.

Chromosome aberations in Chinese hamster ovary cells - positive. ✓

Sister chromatid exchange (SCE) - positive. ✓

NTP Bioassay
Gulf South Research Institute

Rats and mice are being administered EGEE by gavage.

Results should be available in approximately 1 year.

Ethylene Glycol Monobutyl Ether - (EGBE)

SUBCHRONIC

Nagano, et al, (1977, 1979)

Mice received 25 doses of (EGBE) by gavage at levels of 2000, 1000 and 500 mg/Kg.

No effects on testicular weight, germinal cell epithelium or white blood cell count were observed. A reduction in red blood cell count was observed.

No effect level (testicular and white blood cell effects) - 2000 mg/Kg.

Minimal-effect RBC's - 500 mg/Kg.

Dodd, D. E., et al, (1982)

Rats were exposed to (EGBE) vapors at levels of 245, 86 and 20 ppm for 9 days over an 11-day period.

Effects on weight gain, liver weights and red blood cells were observed. No effects on white blood cells, bone marrow or testicular tissue was observed.

No-effect level - 20 ppm.

Dodd, D. E., et al, (1982)

Rats were exposed to (EGBE) vapors at levels of 77, 25 and 5 ppm for 13 weeks.

Effects on red blood cells were seen during the study but no effects were observed at the end of the study. Red blood cell counts, white blood cell counts, testes weight and histopathological examinations were not different from controls.

Minimal-effect level - 77 ppm.

Union Carbide Corporation
Report (1980)

Rabbits received (EGBE) by covered application to the abdominal skin. 1 ml aliquots of solutions of 100%, 50%, 25% or 5% were applied nine times in an 11-day period.

Hemoglobinuria, red blood cell depression and some skin irritation were observed. No other effects were noted.

No-effect level - 25% solution.

Ethylene Glycol Monobutyl Ether - (EGBE)

CMA-Sponsored Study
WIL Laboratories

Rabbits are receiving EGBE by application to the abdominal skin. Dosage levels are 150, 50 and 10 mg/Kg applied as 43%, 14% and 3% solutions. The study will be conducted over a 13-week period.

Results should be available by December, 1982.

TERATOLOGY

CMA-Supported Study
(Bushy Run Research Center)

Female rats and rabbits will be exposed to EGBE vapors over days 6 through 15 (rats) and 6 through 18 (rabbits) of gestation. A probe study will be conducted in pregnant animals of each species to determine appropriate dosage levels.

This study is expected to start in July, 1982. Results should be available in December, 1982.

MUTAGENICITY

Union Carbide Corporation
Report (1980)

Chinese hamster ovary mutation test - negative.

Unscheduled DNA synthesis (UDS) - negative.

Sister chromatid exchange (SCE) - negative.

Ethylene Glycol Ether Acetates

SUBCHRONIC

Nagano, et al, (1977, 1979)

Mice received 25 doses of EGME acetate and EGEE acetate by gavage at levels 2000, 1000, 500, 250, 125 or 62.5 mg/Kg (EGME acetate) or 4000, 2000, 1000 or 500 mg/Kg (EGEE acetate).

Testicular atrophy, germinal cell epithelium damage and depressed white blood cell count were observed.

No-effect level: EGME acetate - 500 mg/Kg

EGEE acetate - 1000 mg/Kg

Truhaut, et al, (1979)

Rats and rabbits were exposed to EGBE acetate vapors at saturation levels for a 1-month period (4 hours/day, 5 days/week).

Hemoglobinuria and/or hematuria, depressed blood cells, and nephrotoxicity were observed. No testicular damage was noted.

No no-effect level determined.

Truhaut, et al, (1979)

Rats and rabbits exposed to either EGEE acetate (200 ppm) or EGBE acetate (100 ppm) for a 10-month period.

No effects on the kidney, no effects on red or white blood cell count, no abnormal urine chemistry or no histopathology.

No-effect levels: EGEE acetate - 200 ppm

EGBE acetate - 100 ppm

TERATOGENICITY

No relevant data

MUTAGENICITY

No relevant data

Other Glycol Ethers

TERATOLOGY

Uemura, K. (1980)

Female mice received ethylene glycol dimethyl ether (glyme) by gavage at levels of 490 mg/Kg, 350 mg/Kg or 250 mg/Kg on days 7 through 10 of pregnancy.

No maternal toxicity was reported. Fetotoxicity, increases in major malformations and skeletal anomalies and delayed ossification were noted.

No no-effect limit established.

Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12454A

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~~ 3 ~~1~~ ~~2~~ pages 1,2 pages _____

Notes:

Contractor reviewer: JW Date: 1/17/96

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: 0992 - 12454 SEQ. A
 Submission # BEHO.

TYPE: INT. SUPP FLWP
 SUBMITTER NAME: Union Carbide Corporation

INFORMATION REQUESTED: FLWP DATE
 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TEC1)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)
 DISPOSITION:
 0505 REFER TO CHEMICAL SCREENING
 0506 CAP NOTICE

VOLUNTARY ACTIONS:
 0401 ACTION REJECTED
 0402 STUDY'S PLAN: DRAINING W. AT
 0403 NOTIFICATION IN WIKI R. 11110 W. AT
 0404 LABELING (THANKS)
 0405 PROCESSIONING (THANKS)
 0406 APP. USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

SUB. DATE: 09/24/92 OTR DATE: 09/29/92 CSRAD DATE: 06/02/95

CHEMICAL NAME: 109-86-4

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	EPICLON	01 02 04	0201 BAWLINO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	HUMAN EXPOS (PROD CONTAM)	01 02 04	0202 BAWLINO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0203 CHEMPHY'S PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	HUMAN EXPOS (MONITORING)	01 02 04	0204 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	ECOAQUA TOX	01 02 04	0205 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	ENV. OCCURRENCE/FATE	01 02 04	0206 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	EMER INCI OF ENV CONTAM	01 02 04	0207 DNA DAMAGE/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	RESPONSE REQUEST DELAY	01 02 04	0208 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	PRODUCING/CHEM ID	01 02 04	0209 MEDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	REPORTING RATIONALE	01 02 04	0210 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	METAPHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	METAPHARMACO (HUMAN)	01 02 04		

TRAJES DATE: YES NON-CELL INVENTORY: YES ONGOING REVIEW: YES (DROPPED) TOXICOLOGICAL CONCERN: LOW PRODUCTION: USE

CAS SR: NO NO (CONTINUE): NO HIGH: HIGH

SEARCH: MUS
RAT
RBT

11) 8EHQ-92-12454: Rank - medium.

Chemical: ethylene glycol monomethyl ether (EGME; CAS# 109-86-4).

Letter from W Kuryla of Union Carbide, Danbury CT, dated September 24, 1992: <no data>: Negative for gene mutations in Salmonella typhimurium.

Equivocal for gene mutations in the Drosophila melanogaster sex-linked recessive lethal (SRL) assay in vivo.

Positive for chromosome mutations (aberrations) in Chinese hamster ovary (CHO) cells in vitro.

Negative for chromosome mutations (aberrations) in rats exposed in vivo.

Equivocal for dominant lethality in rats exposed in vivo.

Does not induce DNA effects in the form of unscheduled DNA synthesis (UDS).

Induces DNA effects in the form of sister chromatid exchanges (SCEs) in CHO in vitro.

Induces spermhead abnormalities in mice exposed in vivo.

12454A

EGME

M

Subacute oral toxicity is of medium concern based on testicular atrophy, germinal cell epithelium damage and depressed red and white blood cell counts in mice exposed to 25 doses of 250, 500, 1000, and 2000 mg/kg. Mice were also exposed to 125 and 62.5 mg/kg. The NOEL was 125 mg/kg.

M

Subacute inhalation toxicity is of medium concern based on toxicity observed in rats and rabbits exposed to 100, 300 and 1000 ppm for 9 days. Testicular atrophy, depressed thymus gland weight, germinal cell epithelium damage, depressed bone marrow cellularity and depressed red and white blood cell counts were observed in both rats and rabbits (≥ 300). The NOEL was 100 ppm.

EGEE

L

Subacute oral toxicity is of low concern based on no deaths in mice exposed to 25 doses of 4000, 2000, 1000 and 500 mg/kg by gavage. Signs of toxicity included testicular atrophy, germinal cell epithelium damage and decreased white blood cell count (≥ 2000). The NOEL was 1000 mg/kg.

EGBE

M

Subacute inhalation toxicity is of medium concern based on effects on weight gain, liver weight and red blood cells in rats exposed to 20, 86, and 245 ppm for 9 days. The NOEL was 20 ppm.

L

Subacute oral toxicity is of low concern based on minimal toxicity in mice exposed to 25 doses of 500, 1000, and 2000 mg/kg. A reduction in red blood cell count was observed. The NOEL (testicular and white blood cell effects) was 2000 mg/kg.

L

Subacute dermal toxicity is of low concern based on minimal toxicity in rabbits exposed to 9

treatments of 5, 25, 50, and 100% solutions over an 11-day period. Hemoglobinuria, red blood cell depression and some skin irritation were reported. The NOEL was 25% solution.

EGME Acetate

L

Subacute oral toxicity is of low concern based on toxicity in mice exposed to 25 doses of 62.5, 125, 250, 500, 1000, and 2000 mg/kg by gavage. Testicular atrophy, germinal cell epithelium damage and depressed white blood cell count were observed (≥ 1000). The NOEL was 500 mg/kg.

EGEE Acetate

L

Subacute oral toxicity is of low concern based on toxicity in mice exposed to 25 doses of 62.5, 125, 250, 500, 1000, and 2000 mg/kg by gavage. Testicular atrophy, germinal cell epithelium damage and depressed white blood cell count were observed (2000). The NOEL was 1000 mg/kg.

EGBE Acetate

ND

Subacute inhalation toxicity concern could not be determined because concentrations were not specified. Hemoglobinuria and/or hematuria, depressed blood cells, and nephrotoxicity occurred in rats and rabbits exposed to saturated vapors for 4 hours/day, 5 days/week for 1 month.