8EHQ-0992-12147

Contains NO CBI

92 SEP 29 AM 10: 09

UNION CARBIDE

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

88920010384

8EHQ-92-12147

September 24, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

8EHQ-92-12147
INIT 10/07/92

88920010384

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

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

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes conclusions from various glycol ether presentations.

"Glycol Ether Symposium", Union Carbide Corporation, Letter from T. R. Tyler to R. C. Wise, October 5, 1983.

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)

gesym

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

UNION CARBIDE CORPORATION
CORPORATE APPLIED TOXICOLOGY
HEALTH, SAFETY AND ENVIRONMENTAL AFFAIRS DEPARTMENT
P. O. BOX 8361, SOUTH CHARLESTON, WV 25303

Mr. R. C. Wise
M-4527
DANBURY/500

Date October 5, 1983

FILE B-2

Dr. Bryan Ballantyne - 511
Mr. M. R. Huffman - 511
Dr. W. C. Kuryla - 511

Subject Glycol Ether Symposium NIOSH

Dear Mr. Wise:

The following is a brief synopsis of what I consider relevant comments on various glycol ether symposium presentations:

SESSION 1: I missed Bryan Hardin's, Dick Smith's and Jim Lyon's presentations.

SESSION 2: Teratology

a) T. R. Hanley
(Dow)

Nothing new but a reasonable presentation of the known EGME effects on reproduction. Fetotoxicity at 3000 ppm PGME accompanied by maternal toxicity. No adverse effects on the fetus at lower levels.

SESSION 3 - Reproduction

a) Bryan Hardin
(NIOSH)

A review of their work on teratology of EGEE, EGEE Acetate, EGBE and DE by dermal application.

EGEE	0.5 ml X 4/day	complete resorptions.
EGEE	0.25 ml X 4/day	embryotoxicity/fetotoxicity.
EGEE ACETATE	0.35 ml X 4/day	fetal effects.
EGBE	0.2 ml X 4/day	necrosis of tail of fetuses.
DE	0.35 ml X 4/day	no effects.

SUMMARY

SESSION 7: Testicular Toxicity

a) Doe
(ICI)

A large number of studies conducted to determine dose response and time course of testicular damage produced by EGME. This was a beautiful piece of work but most of it has been published. The testicular effects of EGME appear to be reversible if dosing stopped before major damage was done to stem cells. At 600 ppm PGME did not produce testicular damage.

b) Foster
(BIBRA [English equivalent of CIIT])

Another beautiful paper on testicular effects of EGME. Mechanistic studies conducted by this group implicate the metabolite, methoxyacetic acid, as the ultimate agent producing the effects on testicular tissue. In this model the parent glycol was without activity. They hypothesize that the aldehyde intermediate may in fact be the molecule of concern with respect to this effect.

215-2-14

UNION CARBIDE INTERNAL CORRESPONDENCE

UNION CARBIDE CORPORATION
CORPORATE APPLIED TOXICOLOGY
HEALTH, SAFETY AND ENVIRONMENTAL AFFAIRS DEPARTMENT
P. O. BOX 8361, SOUTH CHARLESTON, WV 25303

Recvd RRCWise 10/17/83 GO Early FYI McFarland

RECEIVED OCT 11 1983 R. C. W.

me) Mr. R. C. Wise
n M-4527
n DANBURY/500

Date October 5, 1983

FILE B-2

Dr. Bryan Ballantyne - 511
Mr. M. R. Huffman - 511
Dr. W. C. Kuryla - 511

Subject Glycol Ether Symposium NIOSH

Dear Mr. Wise:

The following is a brief synopsis of what I consider relevant comments on various glycol ether symposium presentations:

SESSION 1: I missed Bryan Hardin's, Dick Smith's and Jim Lyon's presentations.

SESSION 2: Teratology

a) T. R. Hanley
(Dow)

Nothing new but a reasonable presentation of the known EGME effects on reproduction. Fetotoxicity at 3000 ppm PGME accompanied by maternal toxicity. No adverse effects on the fetus at lower levels.

b) F. D. Andrew
(Syntex)

A poor presentation of the NIOSH sponsored Battelle data.

c) Walt Krasavage
(Eastman)

Summarized new data on ethylene glycol monopropyl ether. At 400 and 800 ppm maternal toxicity was seen as evidenced by discolored urine and decreased maternal body weight. At 800 ppm there was evidence of fetotoxicity and embryo lethality. Very little effect was seen on the fetus at 400, 200 or 100 ppm.

d) John Doe
(ICI)

Summary of ICI CELLOSOLVE and CELLOSOLVE Acetate studies. He mentioned that CELLOSOLVE Acetate appeared to be 1/2 as potent as CELLOSOLVE. Indicated that Dutch Belted and New Zealand rabbits were about equally sensitive to the developmental toxicity of these compounds. (In private conversations with Dr. Tyl he indicated that he felt the New Zealand rabbits were more sensitive to cardivascular effects. They saw 9 VSD with Dutch Belted versus 35 VSD with New Zealand after subcutaneous injection of EGME).

e) B. K. Nelson
(NIOSH)

A summary of their behavioral work - nothing new.

f) Shelly Tyl
(BRRC)

A summary of the Butyl CELLOSOLVE study - awful slides.

SESSION 3 - Reproduction

a) Bryan Hardin
(NIOSH)

A review of their work on teratology of EGEE, EGEE Acetate, EGBE and DE by dermal application.

EGEE	0.5 ml X 4/day	complete resorptions.
EGEE	0.25 ml X 4/day	embryotoxicity/fetotoxicity.
EGEE ACETATE	0.35 ml X 4/day	fetal effects.
EGBE	0.2 ml X 4/day	necrosis of tail of fetuses.
DE	0.35 ml X 4/day	no effects.

b) Nagano
(Japan)

Read his 1977 and 1979 publications.

c) Clapp
(NIOSH)

Looked for an exposed population. Indicated a sloppy operation in a West Virginia production (or distribution) facility. However, they couldn't find a reasonable exposed cohort.

SESSION 4: Short Term Tests

a) McGregor
(Inveresk)

Reviewed the known mutagenicity of all the glycol ether. Concluded that if they had genotoxic activity, it was certainly weak. The studies were criticized from the floor in that the appropriate activation systems may not have been incorporated into the <u>in vitro</u> test systems.

b) Thompson
(Procto.r and Gamble)

DB not mutagenic in Ames, SCE, tests. Weak response in mouse lymphoma assay. Negative in dropsophila assay.

c) Houchens
(Battelle)

Interesting, but poorly conducted mechanistic study to determine effects of EGME on immune system. If anything, EGME enhanced the immune response of mice to a challenge of tumor cells.

d) Caruso
(Michigan State)

Cell/cell communication model in cultured cells. A good review of the system. All glycol ethers and ethylene glycol inhibited cell/cell communications. She claimed this was indicative of teratogens and carcinogen promoters.

e) Welsch
(CIIT)

Glycol ethers inhibit cell/cell communication but effects are transitory.

f) Marshall Johnson
(Jefferson Medical College)

A superb introduction reviewing teratology concepts followed by a promotional talk on the Hydra model. A/D ratios of glycol ethers vary between 1 and 5. EGEE = 5

g) Schuler
(NIOSH)

A review of results from the NIOSH sponsored Chernoff assay.

SESSION 5: Subchronic and Chronic Toxicity

a) Melnick
(NIEHS)

Preliminary results from EGEE NTP bioassay. Severe toxicity at high level resulted in sacrificing all animals at this level early; not much data obtained. At lower levels, decreased weight gain, dereased testes weight with an indication that EGEE surpressed the normally encountered testicular tumor formation generally seen in 100% of aged Fischer rats. Increased adrenal weights may indicate a problem.

b) Conaway
(Texaco)

A review of the EGEE Biodynamics study that went on and on and on and on and on .....

c) Katz
(Eastman)

A review of their subchrnoic inhalation work with ethylene glycol monopropyl ether. This material appears to produce transitory hemolytic effects on red blood cells, but no testicular or bone marrow effects.

SESSION 6: Percutaneous Absorption

a) Tyler
(UCC)

By far and away the best paper of the Symposium Tyler should receive an accommodation from the American Public. Could go on and on and on and on and on .....(Pulitzer ?)

b) Guest
(Eastman)

Percutaneous absorption of EGEE and EGEE Acetate in dogs. The acetate eliminated more slowly than the parent glycol.

c) Dugard
(ICI)

I missed this paper in order to expedite the issuance of MSDS's on the 24-L Series TERTIGOLS.

SESSION 7: Testicular Toxicity

a) Doe
(ICI)

A large number of studies conducted to determine dose response and time course of testicular damage produced by EGME. This was a beautiful piece of work but most of it has been published. The testicular effects of EGME appear to be reversible if dosing stopped before major damage was done to stem cells. At 600 ppm PGME did not produce testicular damage.

b) Foster
(BIBRA [English equivalent of CIIT])

Another beautiful paper on testicular effects of EGME. Mechanistic studies conducted by this group implicate the metabolite, methoxyacetic acid, as the ultimate agent producing the effects on testicular tissue. In this model the parent glycol was without activity. They hypothesize that the aldehyde intermediate may in fact be the molecule of concern with respect to this effect.

c) Chapin
(NIEHS)

More slides of damaged testicular tissue. This group has been totally upstaged by BIBRA.

d) Zenik
(University of Cincinnati)

His work was completely overewhelmed by that of the previous speakers. EGEE produced reversible testicular damage in rats.

SESSION 8: Metabolism

a) Miller
(Dow)

A rehash of their publication on EGME metabolism compared with PGME metabolism. They show completely different routes of metabolism for the two materials.

b) Plotnick
(NIOSH)

Predominantly a methodology paper where they identify a glycine conjugate of EGEE.

c) Smallwood
(NIOSH)

They discuss methodology whereby analytical determinations of monoalkyl ether acids could be used as biological monitors for glycol ether exposure. The analytical methods are not that great.

SESSION 9: Regulatory Considerations

I missed most of this discussion while attending the needs of a competing Division concerned about submission of a PMN on a glycol ether substitute product.

In addition to the presentations, a number of stimulating conversations were held with other individuals including:

a) Trent Lewis, NIOSH, who suggested we contact William Kelley about our desire to make a presentation to the ACGIH.

b) John Doe and J. P. Lyon who indicated that Peter Selbe of BASF has been commissioned to write the documentation for the German MAC's on glycol ethers.

c) Leddy Terhan of the Section 4 Test Rule Development Branch who indicated, among other things, that final test rules were being developed for DETA.

d) Dr. Phillip T. Goad of Intox Laboratory who indicated that we could get a manuscript concerning the teratology studies they have conducted using brief high exposures to glycol ethers. He might best be contacted through Shelly Tyl, whom he knows personally.

I have attempted to be brief in my summary of this meeting. I hope you find these comments helpful. If you have any questions, do not hesitate to call me.

Sincerely,

Tipton Tyler

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

TRT/nsb
1119T