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I U C L I D

Data Set

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Existing Chemical : ID: 107-30-2

Producer Related Part
Company : The Dow Chemical Company
Creation date : 03.03.2003

Substance Related Part
Company : The Dow Chemical Company
Creation date : 03.03.2003

Memo :

Printing date : 18.12.2003
Revision date :
Date of last Update : 30.07.2003

Number of Pages : 34

Chapter (profile) :
Reliability (profile) :
Flags (profile) : ???

1.0.1 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type : organic
Physical status : liquid
Purity : ≥ 92 - % w/w
Reliability : (2) valid with restrictions
01.04.2003

(1)

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

CAS-No : 542-88-1
EINECS-No :
EINECS-Name : bis (chloromethyl) ether
Contents : $\geq 1 - 8$ % w/w
Remark : According to the American Industrial Hygiene Association, bis(chloromethyl) ether, BCME, is formed inadvertently in the production and use of CMME. In the presence of either hydrogen or hydroxyl ions and traces of water, CMME disproportionates to aldehydes and dimethoxymethane, which, in turn, recombine to form BCME.

04.04.2003

(1)

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

Result : Without establishing a PEL, OSHA identifies CMME as an occupational carcinogen and regulates worker exposure.

1. General Information

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22.04.2003		(2)
Result 22.04.2003	: Category 1, sufficient evidence of carcinogenicity for humans	(3)
Result 22.04.2003	: Carcinogen with no further classification	(4)
Result 22.04.2003	: Group 1, known carcinogen for which there is sufficient evidence of carcinogenicity from studies in humans	(5)
Result 22.04.2003	: A2, suspected human carcinogen	(6)

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Result 04.04.2003	: ACGIH TLV-TWA for bis(chloromethyl) ether is 0.001 ppm (0.0047 mg/m3) A1 (confirmed human carcinogen).	(7)
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1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1. General Information

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1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : = -103.5- °C
Sublimation :
Method :
Year : 1983
GLP : no data
Test substance :
Reliability : (2) valid with restrictions
01.04.2003 (8)

2.2 BOILING POINT

Value : = 59 - °C at
Decomposition :
Method :
Year : 1983
GLP : no data
Test substance :
Reliability : (2) valid with restrictions
01.04.2003 (8)

Value : = 59.5 - °C at
Decomposition :
Method :
Year : 1983
GLP :
Test substance : as prescribed by 1.1 - 1.4
Reliability : (2) valid with restrictions
01.04.2003 (9)

2.3 DENSITY

Type : relative density
Value : = 1.0625 - at 4° C
Reliability : (2) valid with restrictions
09.06.2003 (10)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 162.7 - hPa at 20° C
Decomposition :
Method :
Year : 1977
GLP :
Test substance : as prescribed by 1.1 - 1.4
01.04.2003 (11)

Value : = 286.6 - hPa at 25° C
Decomposition :
Method :

2. Physico-Chemical Data

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Year : 1988
GLP :
Test substance : as prescribed by 1.1 - 1.4
Remark : No further information provided
Reliability : (2) valid with restrictions
01.04.2003 (12)

2.5 PARTITION COEFFICIENT

Log pow : = -.21 - at ° C
Method
Year : 1977
GLP : no data
Test substance :
Remark : Value calculated from the parent solute and the known additive pi constants for substituents or by summation of fragmental constants. No additional information supplied.

Log Kow is probably not applicable due to the rapid hydrolysis of this material.
Reliability : (4) not assignable
4E
20.05.2003 (13)

2.6.1 WATER SOLUBILITY

Remark : At a concentration <50% water solubility (concentration not stated) the half life was 2 minutes.

Water solubility is probably not applicable due to the rapid hydrolysis of this material.
Reliability : (2) valid with restrictions
17.06.2003 (14)

Method :
Year : 1979
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Hydrolyzes rapidly in water with a half life of <1 second.

Water solubility is probably not applicable due to the rapid hydrolysis of this material.
Reliability : (2) valid with restrictions
17.06.2003 (15)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2. Physico-Chemical Data

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2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type : air
Light source :
Light spect. : - nm
Rel. intensity : - based on Intensity of Sunlight
Method : Method of Hendry, D.G. and Kenley, R.A.(1979). Atmospheric reaction products of organic compounds. EPA Report EPA-560/12-79-001 was used.
Result : The atmospheric residence time is expected to be 0.004 - 3.9 days. This is based on theoretically-estimated gas-phase rate constants for the initial reaction between OH radicals and the volatile chemical in units of $10(-12)\text{cm}^3/\text{molecule}/\text{second}$. The Koh rate constant for CMME is estimated to be 3.
Reliability : (2) valid with restrictions
 2E
 30.07.2003 (16)

Type : air
Light source :
Light spect. : - nm
Rel. intensity : - based on Intensity of Sunlight
Result : $1.0 \times 10^{-10} \text{ mol}^{-1} \cdot \text{sec}^{-1}$
Reliability : (2) valid with restrictions
 2F
 30.07.2003 (11)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : - at degree C
t1/2 pH7 : - at degree C
t1/2 pH9 : - at degree C
Deg. Product :
Method :
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Result : Half life is <0.007 seconds in water.
Reliability : (2) valid with restrictions
 2E
 20.05.2003 (17)(11)

Type : abiotic
t1/2 pH4 : - at degree C
t1/2 pH7 : - at degree C
t1/2 pH9 : - at degree C
Result : Chloromethyl methyl ether is hydrolyzed to hydrogen chloride, methanol and formaldehyde.
Reliability : (2) valid with restrictions
 01.04.2003 (18)

Type : abiotic
t1/2 pH4 : - at degree C
t1/2 pH7 : - at degree C
t1/2 pH9 : - at degree C
Method : Known quantities (10-50 ul) were added to a titration vessel containing 10

ml solvent (water:dimethylformamide, 3:1). Hydrolysis and titrations were done in a constant temperature bath at 0C by use of an automatic recording pH titrator (Radiometer Co., Copenhagen, Denmark) set to maintain pH 7.0 by the automatic addition of 2.0N aqueous sodium hydroxide. Pseudo first-order rate constants were calculated from the amount of base added over a known time interval.

Result : The half life was less than 2 minutes.
Reliability : (2) valid with restrictions
2e

02.04.2003

(19)

19.05.2003

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge
Concentration : 100mg/l related to related to
Contact time : 28 day
Degradation : - % after
Result : readily biodegradable
Deg. Product :
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year : 1992
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Based on this data, the test material is considered to be readily biodegradable.
Result : In three replicates of the test, 33, 67 and 76% BOD was observed. These values corresponded to 80, 80 and 83% of the TOC.
Reliability : (2) valid with restrictions
06.06.2003

(20)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3. Environmental Fate and Pathways

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3.8 ADDITIONAL REMARKS

- Memo** : half life in air
Method : Rate of hydrolysis was determined under various experimental conditions using several materials.
- Result** : The rate of hydrolysis ranged between 0.31 - 0.0018 per minute (half lifes ranged from 2.3 - 390 minutes) and was dependent on the surface of the chamber, temperature and relative humidity. As the temperature increased the rate of hydrolysis decreased. This suggests that the hydrolysis reaction occurred on the glass surface instead of in the gas phase. A strong surface effect on the rate of hydrolysis was observed in the following decreasing order: ferric oxide powder -coated Saran > glass >Teflon >Saran. Therefore the hydrolysis half-life in gas phase was greater than or equal to 390 minutes at a relative humidity of 39% at 29C. The rate of hydrolysis was slower at lower relative humidities. Because of the strong surface effect on the rate of hydrolysis of CMME, the material of construction of the analytical devices used had a significant effect on the results.
- Reliability** : (2) valid with restrictions
2E
- 19.05.2003 (21)
- Memo** : Half life in air
Result : Half life is <3.9 days. Hydrolysis products are hydrogen chloride, methanol and formaldehyde.
- 01.04.2003 (22)
- Memo** : Stability in air
Result : Half life in air due to hydrolysis is 3.5 to 6 minutes at 25C.
- 01.04.2003 (23)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50	
Species	:	rat	
Strain	:		
Sex	:		
Number of animals	:		
Vehicle	:		
Method	:		
Year	:	1948	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Chloromethylmethylether was fed as a 10% solution in olive oil to rats.	
Result	:	Animals survived at a single dose of 300 mg/kg whereas 1000 mg/kg caused death.	
		No additional information supplied.	
Reliability	:	(2) valid with restrictions	(24)
01.04.2003			
Type	:	LD50	
Species	:	rat	
Strain	:		
Sex	:		
Number of animals	:		
Vehicle	:		
Value	:	= .21 - ml/kg bw	
Method	:		
Year	:	1969	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Groups of 5 non-fasted Wistar rats, 4-5 weeks of age and 90-120 g in weight were used. Based upon mortalities during a 14-day observation period, the most probable LD50 value and its confidence intervals were estimated by the method of Thompson.	
Remark	:	Based on the specific gravity of 1.0625, 0.21 ml/kg corresponds to 223 mg/kg.	
Result	:	The single dose oral LD50 is 0.21 ml/kg with confidence intervals of 0.12-0.37.	
		No additional information provided.	
Reliability	:	(2) valid with restrictions	(25)
09.06.2003		2E	
Type	:	LD50	
Species	:	rat	
Strain	:		
Sex	:		
Number of animals	:		
Vehicle	:		
Value	:	= 817 - mg/kg bw	
Reliability	:	(4) not assignable	(26)
20.05.2003		4B	

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50	
Species	:	rat	
Strain	:		
Sex	:		
Number of animals	:		
Vehicle	:		
Exposure time	:		
Method	:		
Year	:	1975	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Groups of male Sprague-Dawley rats, approximately 8 weeks old, were exposed for a single 7-hour exposure to 12.5, 26, 42, 54, 70, 141 or 225 ppm chloromethyl methyl ether. Atmospheric analysis of CMME was conducted. Surviving animals were held for 14 days. All animals were necropsied and respiratory tract tissues saved for histopathological evaluation. Lung to body weight ratios were determined and compared to control values.	
Remark	:	Mortality at 26 and 42 ppm is reportedly 110 and 225%, respectively. Obviously this is incorrect. It is not possible to tell what the correct values should be.	
Result	:	<p>Since moisture in air reacts very rapidly with chloromethylmethylether, the concentration to which these animals were exposed to is unknown.</p> <p>The 7-hour LC50 was 55 ppm. All animals died at 70 ppm and higher. Lungs of rats were congested and edematous with evidence of hemorrhage. These gross findings were present to a lesser extent even in animals that survived the 14-day post-exposure period. Acute necrotizing bronchitis was also observed.</p> <p>Based on a large colony control study, the average lung to body weight ratio was approximately 0.6 +/- 0.1 for rats. The authors have considered any values above mean plus 3 SD (0.9) for rats as elevated.</p> <p>Lung to body weight ratios were increased at concentrations of 26 ppm and higher. At 26 ppm, the lung to body weight ratio was 20% greater than control plus 3 SD.</p>	
Reliability	:	No additional information provided. (2) valid with restrictions 2e	
06.06.2003			(27)
Type	:	LC50	
Species	:	rat	
Strain	:		
Sex	:		
Number of animals	:		
Vehicle	:		
Exposure time	:		
Method	:		
Year	:	1948	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Groups of 6 rats were exposed for 30, 60 or 240 minutes to vapor concentrations of 100, 200, 500, 1000, 2000, 5000 and 10,000 ppm.	
Remark	:	Since moisture in air reacts very rapidly with chloromethylmethylether, the concentration to which these animals were exposed to is unknown.	
Result	:	Lethality was observed in rats exposed to 2000 ppm and higher for 30	

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minutes or to 100 ppm and higher for 4 hours.

Deaths resulting from vapor exposure are almost all delayed deaths occurring several days and even weeks after exposure. Most deaths were due to pneumonia.

No additional information provided.

Reliability : (2) valid with restrictions
2E

17.06.2003

(24)

Type : LC50

Species : rat

Strain :

Sex :

Number of animals :

Vehicle :

Exposure time : 4 hour(s)

Method :

Year : 1969

GLP : no

Test substance : as prescribed by 1.1 - 1.4

Method : Groups of 6 rats were exposed to metered vapor concentrations of chloromethylmethylether for 4 hours. Metered vapor concentrations were generated by using various proportioning pumps to meter test material into the air stream prior to entering the chamber. Nominal concentration only was determined. Following the 4-hour exposure period, surviving animals were observed for 14 days.

Remark : Since moisture in air reacts very rapidly with chloromethylmethylether, the concentration to which these animals were exposed to is unknown.

Result : At a nominal concentration of 8 ppm, one of 6 rats died. At 16 ppm, all animals died during the 14-day post-exposure observation period.

Reliability : (2) valid with restrictions
2E

17.06.2003

(25)

Type : LC0

Species : mouse

Strain : Strain A

Sex : male

Number of animals :

Vehicle :

Exposure time : 6 hour(s)

Method : Groups of male mice were exposed for 6 hours to concentrations of CMME ranging from 14.6 - 100 ppm (nominal concentration). Animals were observed for a 14 day post-exposure interval.

Remark : Since moisture in air reacts very rapidly with chloromethylmethylether, the concentration to which these animals were exposed to is unknown.

Result : All animals survived a 6 hour exposure to a nominal concentration of 100 ppm.

Reliability : No further information provided.
(2) valid with restrictions
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(28)

Type : LC50

Species : hamster

Strain :

Sex :

Number of animals :

Vehicle :

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Exposure time	:	
Method	:	Groups of male Golden Syrian hamsters, approximately 6 weeks old, were exposed for a single 7-hour exposure to 12.5, 26, 42, 54, 70, 141 or 225 ppm chloromethyl methyl ether. Surviving animals were held for 14 days. All animals were necropsied and respiratory tract tissues saved for histopathological evaluation. Lung to body weight ratios were determined and compared to control values.
Result	:	<p>The 7-hour LC50 was 65 ppm. All animals died at 225 ppm. Lungs of hamsters were congested and edematous with evidence of hemorrhage. These gross findings were present to a lesser extent even in animals that survived the 14-day post-exposure period. Acute necrotizing bronchitis was also observed.</p> <p>Based on a large colony control study, the average lung to body weight ratio was approximately 0.6 +/- 0.1 for hamsters. The authors have considered any values above mean plus 3 SD (0.8) for hamsters as elevated.</p> <p>Lung to body weight ratios were increased at concentrations of 26 ppm and higher. At 26 ppm, the lung to body weight ratio was 10% greater than control plus 3 SD.</p>
Reliability	:	No additional information provided. (2) valid with restrictions 2e
02.04.2003		(27)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male
Number of animals	:	
Vehicle	:	
Value	:	= .28 - ml/kg bw
Method	:	
Year	:	1969
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	For the dermal LD50 study, groups of 4 male albino New Zealand rabbits weighing 2.5 to 3.5 kg are used. The fur is removed from the entire trunk by clipping, and the dose is retained beneath an impervious plastic film. Animals are immobilized during the 24-hour contact period, after which the film is removed and the rabbits are observed for a 14-day observation period. Based upon mortalities during a 14-day observation period, the most probable LD50 value and its confidence intervals were estimated by the method of Thompson.
Remark	:	Based on the specific gravity of 1.0625, 0.28 ml/kg corresponds to 300 mg/kg.
Result	:	The dermal Ld50 is 0.28 ml/kg with confidence intervals of 0.13 - 0.62).
Reliability	:	(2) valid with restrictions 2E
09.06.2003		(25)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5. Toxicity

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5.2.1 SKIN IRRITATION

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
PDII :
Result :
EC classification :
Method :
Year : 1948
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : One application of undiluted material was made to the rabbit ear. It was also applied to rabbit abdomen.
Result : Severe hyperemia, edema and denaturation was observed on the rabbit ear. Complete destruction of the abdominal wall was observed.

No additional information provided.
Reliability : (2) valid with restrictions
2E

17.06.2003

(24)

Species : rabbit
Concentration : undiluted
Exposure : Open
Exposure time : 24 hour(s)
Number of animals :
PDII :
Result :
EC classification :
Method :
Year : 1969
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Primary skin irritation on rabbits is recorded in a 10-grade ordinal series and is based upon the severest reaction that develops on the clipped skin of each of five albino rabbits within 24 hours of the uncovered application of 0.01 ml of undiluted sample.
Result : Application of 0.01 ml for 24 hour to uncovered rabbit abdomen resulted in necrosis (Grade Level 6).

No additional information provided.
Reliability : (2) valid with restrictions
2E

17.06.2003

(25)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration :
Dose :
Exposure Time :
Comment :
Number of animals :
Result :
EC classification :
Method :

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Year	:	1948	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	A drop of a 1% solution of chloromethyl ether in propylene glycol was placed in the rabbit eye.	
Result	:	The material caused a severe irritation accompanied by extensive necrosis of the eye ball.	
Reliability	:	No additional information supplied. (2) valid with restrictions 2E	
17.06.2003			(24)
Species	:	rabbit	
Concentration	:	undiluted	
Dose	:		
Exposure Time	:		
Comment	:		
Number of animals	:		
Result	:		
EC classification	:		
Method	:		
Year	:	1969	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Eye irritation in rabbits is recorded in a 10-grade ordinal series based upon the degree of corneal necrosis that results from instillations of various volumes and concentrations of test material.	
Result	:	Instillation of 0.5 ml of a 1% solution in water or propylene glycol resulted in a severe burn (Grade Level 10).	
Reliability	:	No further information provided. (2) valid with restrictions 2E	
17.06.2003			(25)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat	
Sex	:	male	
Strain	:	Sprague-Dawley	
Route of admin.	:	inhalation	
Exposure period	:		
Frequency of treatment	:		
Post obs. period	:		
Doses	:		
Control group	:		
Method	:	Thirty day studies on the effects of daily repeated inhalation of CMME were carried out at concentrations of 1 and 10 ppm with 25 rats in each group. Animals that died during the study or survived to the end of the study were subjected to a gross pathological examination. Lung to body weight ratios were calculated and the lungs of animals were examined histopathologically.	
Remark	:	Although not explicitly stated, each exposure was expected to be 7 hours duration.	

Result	: At 10 ppm, the first rats died during the third exposure day and mortality increased progressively to 22 out of 25 animals by the 30th exposure day. The three surviving animals were killed two weeks following the last exposure day. A marked weight decrease was seen in the week immediately following the onset of the exposure, with some indication of recovery toward the end of exposure.	
	For the 9 animals that died within the first ten days of exposure, the average lung to body weight ratio was 1.6. For the 13 animals that died between exposures 11 and 22, the average lung to body weight ratio was 2.2. These are much higher than the control + 3SD value of 0.9. Regenerative hyperplasia of bronchial epithelium was found in 10 of the 25 animals and one animal was found to have squamous metaplasia.	
	At 1 ppm, one animal died on exposure day 16 and 22. Five of the rats surviving 30 exposures were killed at the end of the last exposure and five more were killed two weeks later. The remaining 13 rats were held for lifetime studies. The longest survivor lived for 648 days after the first exposure. Weight change in these animals was not significantly different from that of the controls. Four of the five animals sacrificed after 30 exposures had normal lungs, while one animal had slight bilateral hemorrhage. The animals retained for their life spans showed minimal mucosal effects with two showing regenerative hyperplasia, one squamous metaplasia of the the bronchial epithelium and one tracheal squamous metaplasia.	
	At 10 ppm, measurement for formaldehyde revealed that approximately 50% of the chloromethyl methyl ether was degraded.	
Reliability	: No further information provided. (2) valid with restrictions 2e	
06.06.2003		(27)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	: Bacterial gene mutation assay	
System of testing	:	
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Result	: Chloromethyl methyl ether was positive using genetically well characterized mutants of E coli and S typhimurium.	
	No additional information provided.	
Reliability	: (4) not assignable 4A	
17.06.2003		(29)
Type	: DNA damage and repair assay	
System of testing	:	
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	
Result	: positive	

Method :
Year : 1981
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : A chromosomal aberration test using human lymphocytes was conducted. In this study cells were cultured for a 4 hour period at 37C in humidified atmospheres containing 5% CO2 in presence or in absence of each dose of CMME in sextuplicate samples. In addition, the effects of rat liver phenobarbital induced S-9 mix were also evaluated. Dose levels evaluated were 25, 5 and 10 ul/ml. To measure UDS, 10 mM hydroxyurea was added to each culture to block [3H]-TdR uptake. At the end of the culture period, 3H-TdR uptake by lymphocytes for SDS or for UDS was determined by liquid scintillation counting of 3H activity.
Result : A decrease in the uptake of [3H]-TdR was observed with CMME (Table 1).

Table 1

[3H]TdR uptake by human lymphocytes cultured for a 4 hour period

Compound	[3H]TdR uptake
Control	2661 +/- 57
CMME	856 +/- 9

Without S9 mix the uptake of 3H-TdR was decreased from control values with CMME and hydroxyurea (Table 2). With S9 the uptake of 3H-TdR was increased with CMME and hydroxyurea. Over the concentration range tested, the response was consistent from 2.5 to 10 ul/ml for both with and without S9 activation.

Table 2

[3H]TdR uptake by human lymphocytes cultured for a 4 hour period with hydroxyurea

Compound	[3H]TdR uptake		
	10 ul/ml	5 ul/ml	2.5 ul/ml
Without S9			
Control	715+/-24	715+/-24	715+/-24
CMME	313+/-26	278+/-13	346+/-20
With S9			
Control	612+/-26	612+/-26	612+/-26
CMME	1180+/-33	1320+/-57	1125+/-59

The authors ascribe the high UDS values for CMME could be due to bis(chloromethyl)ether.

Reliability : (2) valid with restrictions
2E

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(30)

Type : Chromosomal aberration test
System of testing :
Concentration :
Cycotoxic conc. :
Metabolic activation : without
Result : positive
Method : other: essentially follows OECD 473
Year : 1996

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GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : No additional information provided.
Result : CMME was positive at 0.015 mg/ml 24 hours after treatment without metabolic activation.
Reliability : (2) valid with restrictions
2E
17.06.2003 (31)

Type : other: adenovirus transformation using hamster cells
System of testing :
Concentration :
Cycotoxic conc. :
Metabolic activation :
Result : positive
Method :
Year : 1980
GLP :
Test substance : no data
Method : Primary cell cultures of Syrian hamster embryo cells (HEC) were prepared. Following 3 to 4 days of incubation at 37C, each of two dishes of cells were treated for 2 or 18 hours with at least 5 dilutions of test chemical, rinsed and inoculated with SA7. After 3 hours of virus absorption, the cells were removed from the dish, centrifuged and resuspended in complete medium. Cells were maintained for 21-25 days at which point they were formalin fixed and stained with Giemsa stain. The SA7-transformed foci were easily identified by their unique morphology.
Result : A positive response was observed with a 10% concentration.
No additional information provided.
Reliability : (3) invalid
3A
17.06.2003 (32)

5.6 GENETIC TOXICITY 'IN VITRO'

Type : Micronucleus assay
Species : mouse
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :
Result : ambiguous
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Groups of 5 male mice were treated by ip injection once with CMME at dose levels of 0, 25, 50 and 100 mg/kg. Samples of bone marrow or peripheral blood were evaluated.
Result : Inconclusive results were obtained with CMME (Table 3). Although some samples showed statistically significant positive responses, the results were considered inconclusive due to the poor reproducibility.

Table 1
Summary of micronucleus assay results for
chloromethylmethyl ether

strain	tissue	dose (mg/kg)	Percent MNPCE or MNRET	
			24 hr	48 hr
CD-1	pb	0	0.18+/-0.09	
		25	0.22+/-0.08	0.22+/-0.14
		50	0.38+/-0.12	0.28+/-0.14
		100	0.55+/-0.13	0.26+/-0.25
CD-1	bm	0	0.36+/-0.17	
		25	0.22+/-0.26	0.34+/-0.21
		50	0.20+/-0.14	0.14+/-0.05
		100	0.54+/-0.39	0.40+/-0.25

pb - peripheral blood

bm - bone marrow

Table 2

Summary of micronucleus assay results for
chloromethylmethyl ether

strain	tissue	dose (mg/kg)	Percent MNPCE or MNRET	
			24 hr	48 hr
CD-1	pb	0	0.14+/-0.13	
		25	0.25+/-0.10	0.28+/-0.17
		50	0.52+/-0.24	0.40+/-0.25
		100	1.04+/-0.73	0.34+/-0.23
CD-1	bm	0	0.16+/-0.11	
		25	N.D.	0.30+/-0.16
		50	0.13+/-0.05	0.32+/-0.15
		100	0.50+/-0.08	0.38+/-0.23

pb - peripheral blood

bm - bone marrow

N.D. – No Data

Table 3

Summary of micronucleus assay results for chloromethylmethyl ether in
peripheral blood of ICR mice

dose (mg/kg)	Percent MNPCE or MNRET			
	0	24	48	72
25	0.24+/-0.16	0.33+/-0.18	0.23+/-0.03	0.25+/-0.09
50	0.24+/-0.13	0.29+/-0.09	0.33+/-0.17	0.19+/-0.05
100	0.35+/-0.09	0.36+/-0.16	0.35+/-0.00	0.40+/-0.09

Test substance

Reliability

17.06.2003

: Authors used reagent-grade CMME with a purity of 95.7%.

: (2) valid with restrictions

2E

(33)

5.7 CARCINOGENITY

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period :
Frequency of treatment :
Post. obs. period :
Doses : 1 ppm

5. Toxicity

Id 107-30-2

Date 18.12.2003

Result	:		
Control group	:	yes, concurrent no treatment	
Method	:		
Year	:	1975	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Groups of 74 male Sprague-Dawley rats were exposed to 0 or 1 ppm chloromethyl methyl ether for 6 hours/day, 5 days/week for a lifetime. By the end of the study, rats had received as many as 565 exposures over a period of 852 days. At the time of necropsy, lungs of animals were removed and filled with 10% neutral buffered formalin. Lungs were stained with hematoxylin-eosin and examined histopathologically.	
Result	:	Mortality and body weight gain were comparable between rats from the control and 1 ppm groups. Histologic changes in the trachea and bronchi were observed in rats exposed to 1 ppm. Treatment-related changes included tracheal squamous metaplasia and bronchial hyperplasia. A squamous cell carcinoma of the lung was discovered in an animal dying at 700 days. An animal dying at 790 days was found to have esthesioneuroepithelioma of olfactory epithelium.	
Reliability	:	No additional information provided. (2) valid with restrictions 2E	
17.06.2003			(34)
Species	:	hamster	
Sex	:	male	
Strain	:		
Route of admin.	:	inhalation	
Exposure period	:		
Frequency of treatment	:		
Post. obs. period	:		
Doses	:		
Result	:		
Control group	:		
Method	:		
Year	:	1975	
GLP	:	no	
Test substance	:	as prescribed by 1.1 - 1.4	
Method	:	Groups of 90 male Golden Syrian hamsters were exposed to 0 or 1 ppm chloromethyl methyl ether for 6 hours/day, 5 days/week for a lifetime. By the end of the study, hamsters had received as many as 565 exposures over a period of 852 days. At the time of necropsy, lungs of animals were removed and filled with 10% neutral buffered formalin. Lungs were stained with hematoxylin-eosin and examined histopathologically.	
Result	:	Mortality and body weight gain were comparable between rats from the control and 1 ppm groups. Histologic changes were observed in the lung of hamsters. Nine animals had bronchoalveolar metaplasia and ten were seen with atypical alveolar cells. Atypical alveolar cells indicates the presence of large, bizarre, pleomorphic, angular and hyperchromatic nuclei. An adenocarcinoma of the lung was found in an animal sacrificed at 134 days after 90 exposures. Additionally, a squamous papilloma of the trachea was seen in an exposed animal that died after 683 days.	
Reliability	:	No additional information provided. (2) valid with restrictions 2E	
17.06.2003			(34)
Species	:	mouse	
Sex	:	male	

5. Toxicity

Id 107-30-2

Date 18.12.2003

Strain : Strain A
Route of admin. : inhalation
Exposure period : 6 hrs/day, 5 days/week for 21 weeks
Frequency of treatment :
Post. obs. period :
Doses : 2 ppm (nominal)
Result :
Control group : yes
Method :
Year : 1971
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : The vapor atmosphere of CMME was obtained by metering the liquid compound with a precision syringe into the air stream entering the chamber to obtain the desired nominal concentration. The analytical concentration was not determined. A group of 50 treated animals was exposed for 6 hrs/day, 5 days/week for 101 days in 21 weeks. A group of 50 control animals was exposed to room air for 6 hrs/day, 5 days/week for 130 days in 28 weeks. During the in-life portion of the study, the animals were observed and weighed. All animals which died during the exposure period were examined. At the termination of the studies, all survivors were killed. Lung specimens from all animals were preserved in formaldehyde solution and examined for tumors. The number of tumors in the lungs was counted and the ratios of the average number of tumors per animal between the treated and the control group was calculated. A ratio of two or greater is considered to be a positive response.

Remark : Since moisture in air reacts very rapidly with chloromethylmethylether, the concentration to which these animals were exposed to is unknown.

Result : There were no effects on mean body weight and demeanor of animals exposed to CMME. Four animals died of unknown causes. Gross necropsies of the dead and the survivors revealed lung abnormalities in 37 animals. Of the 37 animals, 25 also had lung tumors. The average number of tumors per tumor-bearing animal was 3.1 and the mean number of tumors for the group was 1.53.

Test substance : Test substance defined as industrial grade sample. No further information provided.

Reliability : (2) valid with restrictions
2E

17.06.2003

(28)

Species : mouse
Sex : male/female
Strain : SKH/HR1
Route of admin. :
Exposure period :
Frequency of treatment :
Post. obs. period :
Doses :
Result :
Control group :
Method :
Year : 1969
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : ICR Swiss mice 24-72 hours old and weighing an average of 2 g, received a single subcutaneous injection of the vehicle or experimental chemical. The maximum tolerated dose (85% survival 30 days posttreatment) was determined for each compound in a preliminary dose-range study.

Industrial grade bis(chloromethyl)ether and chloromethyl methyl ether were

used. The concentration of BCME in CMME was 0.3% at the beginning of the study and 2.6% at the end of the study. Urethan (ethyl carbamate) was used as a positive control. The vehicle control animals received 0.05 ml peanut oil.

Animals were weaned at approximately 30 days of age and housed individually in hanging wire cages. They were observed daily for mortality and weekly for gross effects. Body weights were recorded monthly. Animals which died during the study were necropsied, and all animals were sacrificed 6 months after compound administration.

Lungs were fixed in Tellyesniczky's fluid. The 5 lobes were examined individually with a dissecting microscope, and the lung adenomas were identified and counted. Representative adenomas were sectioned and examined for histopathologic confirmation and characterization of the lesions. Other grossly abnormal tissues were fixed in 10% formalin and examined.

Result : The number of animals with adenomas was increased slightly in males and females receiving CMME.

Table 1

Compound	Dose/kg	Number	Sex	Number animals w adenomas	Total number of adenomas
Peanut oil	25 ml	20	F	5	5
		30	M	2	2
Urethan	1500 mg	25	F	25	454
		25	M	25	402
BCME	12.5 ul	50	F	20	23
		50	M	25	41
CMME	125 ul	48	F	8	9
		51	M	9	12

Reliability : (2) valid with restrictions
2E

17.06.2003

(35)

Species : mouse

Sex :

Strain : Swiss

Route of admin. :

Exposure period :

Frequency of treatment :

Post. obs. period :

Doses :

Result :

Control group :

Method :

Year : 1969

GLP : no

Test substance : as prescribed by 1.1 - 1.4

Method : Groups of 20 mice were treated with benzo[a]pyrene (B[a]P), CMME or nothing as initiators and acetone, phorbol esters (PE), CMME or nothing as promotors. For the initiation phase, mice were treated once with doses as detailed in Table 1. For the promotion phase, mice were treated three times/week beginning 14 days after the initiation phase. Treatment of all animals was discontinued after 325 days but the animals were maintained

Result : and observed for the duration of the experiment, 540 days.
: Chloromethyl methyl ether applied on mouse skin as a 2% solution in benzene, 0.1 ml/application, i.e., 2 mg of CMME/application, was inactive as a carcinogen.

It proved to be an initiating agent at both 1000 and 100 ug doses with phorbol ester as the promotor, with 5/20 and 7/20 animals, respectively, bearing papillomas and 1/20 and 4/20, respectively, bearing squamous carcinomas (Table 1). The time to first tumor was 140 days with the 1000 ug dose of CMME as initiator whereas the 100 ug dose resulted in a latent period of 259 days.

Table 1
Incidence of skin tumors following various applications of CMME

	Dose mg/ Initiator	Dose mg/ Promotor	Dose mg/ 0.1ml	Number of papillomas	Number of squamous carcinomas
	None	None		0	0
	None	CMME	2.0	0	0
CMME	0.1	None		0	0
CMME	1.0	None		0	0
CMME	1.0	Acetone	0.1	0	0
CMME	0.1	PE	0.025	7	4
CMME	1.0	PE	0.025	5	1
B[a]P	0.15	CMME	2.0	1	0

Reliability : (2) valid with restrictions
2E

17.06.2003

(36)

Species : mouse
Sex : female
Strain : Swiss Webster
Route of admin. : s.c.
Exposure period :
Frequency of treatment :
Post. obs. period :
Doses :
Result :
Control group :
Method :
Year :
GLP :
Test substance :
Method :

: Groups of 30 female Swiss mice received subcutaneous injections once/week on the left flank for their lifetime. The vehicle used was purified paraffin oil. Animals were weighed regularly and examined once a month for palpable masses at the injection site. Mice observed with tumors for two months or moribund were necropsied. Routine sections were obtained of the injection site as well as any other gross abnormalities.

Result : Ten sarcomas were observed at the injection site. There was no significant incidence of tumors at other sites. The first tumor was observed 308 days after the first dose. The median survival time was 496 days.

Reliability : No additional information provided.
: (3) invalid
3B

17.06.2003

(19)

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Memo : epidemiology study
Method : A historical prospective epidemiology study was conducted on workers exposed to chloromethyl methyl ether (CMME). Production workers employed at any time between 1948 and 1972 were followed. The total cohort of 2285 consisted of 669 men believed to have had exposure to CMME plus a nonexposed group of 1616 men from production operations in other sections of the same plant. Supervisory personnel associated with manufacture and use of CMME during the study period ranked the exposure of all job classifications at risk, whether or not a particular job was directly involved in the CMME operations. Any particular job was rated on a severity scale of 0 to 6. The total exposure time for each member of the cohort was also determined.

The Maher paper followed this cohort to Dec 31, 1981, an additional 9 years. In addition, short-term employees previously excluded from the cohort have been added.

Remark : Studies by Figueroa et al., (1973), Weiss and Boucot (1975), DeFonso and Kelton (1976), Pasternack, Shore and Albert (1977) and Collingwood, Pasternack and Shore (1987) were conducted on part of the same population.

Result : Results based on DeFonso paper:
 The 669 men employed in the CMME industry had a combined 11,087 man-years. A total of 19 lung cancer cases were observed when 5.0 were expected based on rates in unexposed production workers. This resulted in an SMR for the exposed population of 3.8.

For the entire exposure group, there was also significantly higher relative risks for workers in the intermediate exposure level with a total exposure time of 5 or more years and in the high exposure level with a total exposure time of 1 or more years.

Results based on Maher paper:
 Of the 737 men employed in the CMME industry, there were 32 observed cases of respiratory tract cancer vs 11.5 expected for an SME of 2.79.

Results based on Maher paper: This is a later follow-up study to the DeFonso paper and follows essentially the same group of workers through 1981. Short-term employees previously excluded from the cohort have been added, and follow-up has been extended an additional 9 years. Thus the population was 737 exposed and 2120 unexposed workers. Mortality from cancer of the respiratory was 2.79 fold greater than expected (32 observed; 11.5 expected).

Reliability : (2) valid with restrictions
 2E

17.06.2003

(37) (38)

Memo : epidemiology study

Method	: A prospective study of 125 chemical workers was carried out for 10 years (Dec 31, 1962 to Dec 31, 1972) to investigate the incidence of lung cancer. Seventy percent of the 125 men were aged 30 to 49 years at the start of the study. Ten percent had never smoked; 8% smoked cigars or pipe only; 5% were ex-smokers of cigarettes and 78% were current cigarette smokers. Twenty four percent smoked more than one pack per day.	
	Fourteen men left the investigation at various intervals during the five -year screening study because of job terminations. However, the survival status of 120 men among the 125, as of Dec 31, 1972, was determined through follow-up.	
	Workers were screened by means of chest photofluorograms and questionnaires regarding age, smoking habits and respiratory symptoms, at intervals averaging 8.5 months.	
Remark	: Exposure data was calculated as by DeFonso and Kelton (1976). : Studies by Figueroa et al., (1973), Weiss and Boucot (1975), DeFonso and Kelton (1976), Pasternack, Shore and Albert (1977) and Collingwood, Pasternack and Shore (1987) were conducted on part of the same population.	
Result	: The incidence of small -cell carcinomas correlated with exposure index (time-weighted exposure rating multiplied by years of exposure from 1948 to 1972) and occurred in relatively young men. The study population did not develop cancer when the exposure index was less than 13.0. At an exposure index of 13.0-24.9, 17.2% developed cancer while at an exposure index >25.0, 30% developed cancer. Symptoms of chronic bronchitis were reported more often among men exposed to CMME and a dose-response relationship was apparent with smoking a cofactor. Ventilatory function was not significantly affected by chemical exposure. Periodic screening over the first five years of the study showed a decrease in chronic coughing and an increase in dyspnea while chemical exposure was diminishing.	
Reliability	: (2) valid with restrictions 2E	
17.06.2003		(39)
Memo Remark	: epidemiology study : Studies by Figueroa et al., (1973), Weiss and Boucot (1975), DeFonso and Kelton (1976), Pasternack, Shore and Albert (1977) and Collingwood, Pasternack and Shore (1987) were conducted on part of the same population.	
Result	: A group of 125 men were studied beginning in Dec 1962 and followed for 5 years. Fourteen men were lost at various intervals because of job termination. In four of the remaining 111 men, lung cancer developed during the five-year period of observation. Eighty eight were in the age group from 35 to 54 and all four cases of lung cancer occurred in this group, giving a five-year incidence of 4.54%.	
	Concurrently a retrospective investigation of 14 lung cancers of workers exposed to chloromethyl methyl ether was made. Hospital records and autopsy results were examined and family physicians were interviewed. Ten of the 14 men smoked one package of cigarettes or more per day. One man smoked pipes only and three had never smoked. Histologic examination of 13 of the 14 lung cancers. Oat-cell carcinoma was found in 12 of 13 lung cancers examined histologically. The remaining individual had a squamous-cell carcinoma. This individual had only been exposed to CMME for one month according to a surviving co-worker. According to the company, this individual had no known exposure.	
Reliability	: (2) valid with restrictions 2E	
17.06.2003		(40)

Memo Method : epidemiology study
 : A retrospective cohort mortality study was conducted on 6152 chemical workers (2460 exposed and 3692 nonexposed) engaged in chloromethyl ether manufacture. The cohort was composed of workers from 7 major U.S. companies from 1948 through 1980. Demographic information and work histories were obtained. Information on workers' smoking history was also requested.

Only two of the 7 companies had measured air concentrations of CMME. Despite the paucity of air concentration data, a rank order estimate of exposure intensity (i.e., score) by job classification was developed at each company. The exposure classification scheme reflected changes in CMME manufacturing processes, these changes impacting exposure levels at each company. Factors considered in the assignment of exposure scores included the changing proximity of jobs in relation to CMME operations, degree of enclosure, production-schedule frequency and quantity and prevailing wind patterns or air movement. It was not possible to assign actual concentrations to exposure scores or define relative differences between companies.

Remark : Studies by Figueroa et al., (1973), Weiss and Boucot (1975), DeFonso and Kelton (1976), Pasternack, Shore and Albert (1977) and Collingwood, Pasternack and Shore (1987) were conducted on part of the same population.

Result : A total of 90 respiratory cancer deaths were observed, including 52 CMME exposed workers and 38 CMME nonexposed workers. Among 32 exposed cases with respiratory cancer deaths with verifiable cell type, the highest proportion of cell types was oat cell (38%). In 20 nonexposed cases with respiratory cancer deaths, the highest proportion was adenocarcinoma (31%).

An increased incidence of respiratory cancers was observed at 2 of the 7 plants. These two plants were two of the three largest production facilities in this study. The third company was recognized as having a superior industrial hygiene program.

Reliability : (2) valid with restrictions
2E

17.06.2003

(41)

Memo Method : epidemiology study
 : A retrospective cohort mortality study was conducted on 10697 chemical workers (1827 exposed and 8870 nonexposed) engaged in chloromethyl ether manufacture. The cohort was composed of workers from 6 major U.S. companies from 1948 through 1972. Vital status and work histories were obtained. Of the 133 CME-exposed workers that have died, death certificates were obtained for 20 individuals.

Remark : Studies by Figueroa et al., (1973), Weiss and Boucot (1975), DeFonso and Kelton (1976), Pasternack, Shore and Albert (1977) and Collingwood, Pasternack and Shore (1987) were conducted on part of the same population.

Result : Nearly half of the workers were employed at Firm 2.

An increased incidence of respiratory cancer and all malignant cancers was observed from Firm 2. This also resulted in an increased number of all malignant cancers for the total cohort. However the observed incidence of respiratory cancers and total malignant cancers at Firms 1, 3-6 was equal to the expected incidence.

Reliability : (2) valid with restrictions
2E

17.06.2003

(42)

Memo : Case report

Result : A case report of a chemist working with bis(chloromethyl) ether and CMME died 12 years after the last exposure to either material at the age of 42. The concentration of either material the chemist was exposed to is unknown. The cancer appeared to be a type papanicolaou V.

Reliability : (2) valid with restrictions
2E

17.06.2003 (43)

Memo Method : epidemiology study
: A cohort study was conducted among workers potentially exposed to CMME in a factory. The cohort consisted of all males employed at this factory between 1958 and December 31, 1986. A total of 1203 men, 258 (with 3785 person-years at risk) had worked in anion-exchange resin manufacture and had documented potential CMME/BCME exposure, while 945 (with 12,136 person-years) were never exposed. 92.2% of exposed and 87.5% of nonexposed workers were accounted for. Potential confounders were not examined in this study. Based on work histories, workers were rated on a scale of 0 to 6 in order of increasing magnitude. Cumulative dose was determined for each worker based on the score derived from the workers exposure history and years worked at that rating.

Result : The lung cancer incidence of workers exposed to CMME/BCME was increased (Table 1).

Table 1
Incidence rates of lung cancer in workers in an anion-exchange plant

Median Cumulative Dose	Number of cases	Person years	SMR
0.5	0	341	0
2.5	1	1001	2.8
6.3	2	1034	4.9
12.5	2	746	16.7
24.0	2	254	40.0
40.0	4	408	18.2
Total	11	3784	

Cumulate dose = Sum of (exposure rating x years at that rating)

Reliability : (2) valid with restrictions
2E

23.04.2003 (44)

Memo Method : epidemiology study
: A cohort study was conducted of 915 individuals from 11 plants which produced and/or processed chloromethyl ether in 8 cities in China. There were 534 males and 381 females in this cohort. These individuals were followed from the beginning of exposure to Dec 31, 1981 which resulted in 9707.5 person-years (6183 males and 3524.5 females).

The SMR of all causes of death was calculated on the basis of statistics of Shanghai.

Remark : The data used to calculate the SMR was from the city of Shanghai which may or may not be representative of other areas of China.

Result : Thirty two deaths occurred during the study period. Among the fatalities, 20 were due to cancer in which 15 were lung cancer. In 11 of the 15 lung cancer cases, histopathological examination of the lung was performed. Of these 11, 8 (73%) were undifferentiated cell cancers and the remaining 3 were squamous cell carcinoma. The average age of death was 50 with a range of 32 - 64. The interval from the year starting work to the diagnosis of lung cancer was 10 with a range of 2-20. The period of survival from

diagnosis was 11.1 months on average with a range of 1-57 months. For the individuals with undifferentiated cell lung cancer the average survival period was 4.7 months.

Of the 8 plants examined, only 3 plants had an observed lung cancer with 12 lung cancers observed in one plant. Six of 14 lung cancer cases were non-smokers (no indication give of the history of 15th person).

The SME for all causes of death was 197 (95% CI 130 - 300) compared to Shanghai.

Reliability : (2) valid with restrictions
2E
19.05.2003 (45)

Memo Method : peripheral lymphocytes
: As part of regular medical check-ups, cytogenetic analysis of peripheral lymphocytes was conducted in workers.

Result : A group of 12 workers with immunological changes also had cytogenetic analysis of peripheral lymphocytes. Scoring 200 cells/person an average of 6.7% aberrant cells were observed. Control values were only 2%. A repeat analysis was conducted in 10 of these 12 workers following their return from holiday. Cytogenetic analysis revealed only 3.1% aberrant cells following holiday.

No further information provided.

Reliability : (4) not assignable
4a
01.04.2003 (46)

Memo Method : peripheral lymphocytes
: Blood samples were obtained from 77 workers occupationally exposed to bis(chloromethyl) ether and chloromethyl methyl ether. Simultaneously synthetic resin workers and subjects without any occupational exposure were used as controls.

After initial samples, workers were given ascorbic acid at daily doses of 1 g, 5 days/week for 5 months and percentage of chromosomal aberrations in peripheral blood was measured.

Result : In the initial sample, the percentage of chromosomal aberrations was increased from control values prior to treatment with ascorbic acid (Table 1). After the 5 month treatment with ascorbic acid, the level had decreased but were slightly greater than control values.

Smoking habits had no clear cut effect on detected changes

Table 1
Effects of ascorbic acid treatment on chromosomal aberrations in BCME and CMME workers

	Initial sample	Final sample
Control	1.64%	1.88%
Synthetic resins workers	3.65%	3.52%
BCME and CMME workers	3.73%	2.13%

Reliability : (2) valid with restrictions
2E
18.06.2003 (47)

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7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT