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**HIGH PRODUCTION VOLUME (HPV)  
CHEMICALS CHALLENGE PROGRAM**

**TEST PLAN**

**For**

**CHLOROMETHYL METHYL ETHER**

**CAS NO. 107-30-2**

**Prepared by:**

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## EXECUTE SUMMARY

The Dow Chemical Company voluntarily submits the following screening information data and Test Plan covering the chemical Chloromethyl Methyl Ether, also known as CMME (CAS No. 107-30-2), for review under the Environmental Protection Agency's High Production Volume (HPV) Chemicals Challenge Program. The Dow Chemical Company, believing there were other producers, attempted to form a consortia with other producers to better document the uses and exposure conditions for this chemical. We were unable to find any additional producers. Thus, Dow Chemical has completed the test plan and submitted the finalized documents for the US HPV program based on our uses of this material.

A substantial amount of data exists to evaluate the potential hazards associated with CMME. Use of key studies or estimation models available from data already developed provide adequate support to characterize all but five endpoints in the HPV Chemicals Challenge Program. The five endpoints for which no data presently exists are aquatic toxicity studies in fish, daphnia and algae and reproduction and developmental toxicity. Based on the uses and extremely rapid degradation of this material in water, these toxicity studies are considered to be unnecessary.

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# TEST PLAN FOR CHLOROMETHYL METHYL ETHER

CAS Nos. 107-30-2

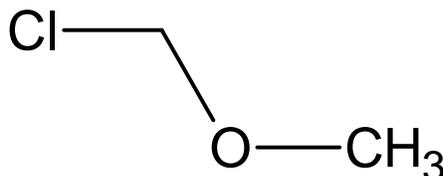
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## I. INTRODUCTION AND IDENTIFICATION OF CHEMICAL

Under EPA's High Production Volume (HPV) Chemicals Challenge Program, The Dow Chemical Company (Dow) has committed to voluntarily compile basic screening data on Chloromethyl Methyl Ether (CMME). The data included in this Test Plan provide physicochemical properties, environmental fate, and human and environmental effects of CMME, as defined by the Organization for Economic Cooperation and Development (OECD). The information provided comes from existing data developed by or on behalf of Dow or found in the published scientific literature.

### A. Structure and Nomenclature

Following is a structural characterization of CMME and associated nomenclature.



Chloromethyl Methyl Ether  
CAS No. : 107-30-2  
Synonyms: CMME

### B. Manufacturing & Use

The Dow Chemical Company operates a single manufacturing site producing CMME. The manufacturing operation is a closed, batch process. During production, methanol, formaldehyde and HCl are reacted together using a catalyst. Following the reaction, CMME is removed from the reactor and piped directly to the ion exchange resin plant located next to the CMME plant where it is used to make ion exchange resins. All CMME produced is used within the ion exchange plant.

Bis Chloromethyl ether (BCME) may be formed following the production of CMME. CMME can hydrolyze in the presence of water to release methanol, formaldehyde and HCl. These molecules can rearrange forming BCME. However, every effort is made to minimize exposure of CMME to moisture. Indeed, technical grade material from the 1970s and 1980s was reported to contain 1-8% BCME when analyzed for toxicity studies. However, these samples were analyzed weeks to months after production

and it is unclear from these reports whether newly manufactured CMME in the 1970 and 1980s also contained this high of a level of BCME. Current production material contains much lower levels of BCME.

Only a few employees are involved in the manufacture of CMME and have extremely low potential for skin and airborne exposure, which occurs chiefly during sampling and material transfer operations. Due to the acute and chronic hazards associated with exposure to CMME and BCME, a known impurity in technical grade CMME, occupational exposure limits of 100 ppb (Dow Industrial Hygiene Guideline) and 1 ppb (ACGIH TLV), respectively, have been set. This has resulted in specific manufacturing procedures and practices to minimize the exposure potential to CMME.

CMME is used internally to produce ion exchange resins and it is utilized exclusively in closed systems. Occupational exposure during processing or use would primarily occur during sampling, material transfer, or, in the unlikely event, that there is an unplanned event. Given the relatively high vapor pressure of this material, every effort is made to minimize loss to the atmosphere during manufacturing or processing. Whenever exposure is possible, personal protective equipment (PPE) and self-contained breathing apparatus (SCBA) equipment is worn to minimize exposure even further.

The only potential exposure to CMME occurs during routine sampling from the reactor for quality control purposes. This sample is then analyzed in the quality control lab. Engineering controls and administrative controls for this task are significant. The sample of CMME is obtained in an enclosed ventilated box which surrounds the sampling apparatus. While obtaining the sample, operations personnel wear the appropriate chemical protective clothing and utilize supplied air respiratory protection. During sample analysis, similar PPE is worn (including an airline respirator) and the sample is analyzed in a typical laboratory fume hood.

For non-routine maintenance tasks such as line and equipment openings, a water flush is performed on the equipment which breaks down the CMME within seconds to HCl, methanol and formaldehyde. In the extremely rare instance where a water flush has not been performed, PPE as described above is worn.

Release of CMME in the plant is closely monitored. A continuous leak detection system is used for the early indication of a potential leak in the process areas handling CMME. Multiple systems are in place, each sampling multiple points throughout the process for the presence of CMME. The systems have a detection limit of 5 ppb for CMME and a building alarm will notify individuals of a release at 50 ppb (Dow IHG is 100 ppb). In the event of a building alarm activation, the plant immediately goes on alert with workers assembling in designated safe areas, ventilation systems are shut down and workers 'shelter in place'. A team of emergency responders suit up with appropriate PPE, including SCBA, and determine the source of the leak. Additional response procedures may then be executed.

A review of full-shift and short term monitoring data (1981 to current) for potential exposure to CMME and BCME indicate that potential exposures are below established exposure guidelines.

## II. TEST PLAN RATIONALE

The information obtained and included to support this Test Plan has come from either:

- 1) Internal studies conducted by/or for Dow

- 2) Studies that have been extracted from the scientific literature either as primary references or as found in well-accepted, peer-reviewed reference books, or
- 3) Studies that were estimated using environmental models accepted by the US EPA (1999b).

This assessment includes information on physicochemical properties, environmental fate, and human and environmental effects associated with CMME. The data used to support this program include those Endpoints identified by the US EPA (1998); key studies have been identified for each data Endpoint and summarized in Robust Summary form and included in Section VII. of this Dossier.

All studies were reviewed and assessed for reliability according to standards specified by Klimisch *et al* (1997), as recommended by the US EPA (1999a). The following criteria were used for codification:

1. Valid without Restriction - Includes studies which comply with US EPA and/or OECD-accepted testing guidelines, which were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented,
2. Valid with Restrictions – Includes studies which were conducted according to national/international testing guidance and are well documented. May include studies conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters which are well documented and scientifically valid but vary slightly from current testing guidance. Also included were physical-chemical property data obtained from reference handbooks as well as environmental endpoint values obtained from an accepted method of estimation (i.e. EPIWIN).
3. Not Valid – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or where documentation is insufficient.
4. Not Assignable – Includes studies in which limited data is provided.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this Dossier. In one case a positive response was reported in two Ames tests. One study was reported as an abstract and the second study was summarized by IARC as positive in the Salmonella assay. Both of these studies were assigned a Klimisch rating of 4. Given the supporting animal carcinogenicity and human epidemiology data available, these studies were considered acceptable for one end point in the HPV program and no additional testing is necessary.

### III. TEST PLAN SUMMARY AND CONCLUSIONS

**Physical-chemical property** values (Melting Point, Boiling Point and Vapor Pressure) were considered to be acceptable.

**Environmental Fate** values for Transport (Fugacity) and Photodegradation were obtained using computer estimation –modeling programs. Biodegradation and Hydrolysis data were considered to be acceptable. The half-life of CMME in water is less than one second at 25C and pH 7.

**Ecotoxicity** studies have not been conducted in aquatic organisms. CMME is rapidly hydrolyzed to HCl, methanol and formaldehyde. Aquatic toxicity studies in fish, daphnia and algae are available for each hydrolysis product with the exception of an algae study with HCl. However, HCl toxicity for algae is most likely associated with pH changes and thus additional studies are unnecessary.

**Mammalian Toxicity** Endpoints (Acute Toxicity, Repeated Dose Toxicity, Ames Mutagenicity and Chromosomal Aberration Testing) have all been considered adequate. Since the most likely route for human exposure is the inhalation route and CMME is rapidly hydrolyzed to HCl, methanol and formaldehyde, it is extremely unlikely that CMME would reach the reproduction organs and/or a developing fetus. Developmental and reproduction toxicity data are available for each hydrolysis product. The hydrolysis product with the lowest NOAEL is formaldehyde, with a NOAEL of 8 ppm for reproductive organs based on a 90 day inhalation toxicity study. These concentrations are much higher than the current Dow IHG for CMME and based on the work of Drew et al., 1975, exceed the concentration one would select for a developmental and/or reproduction toxicity study. Thus no further testing is considered necessary.

A tabular depiction of data availability and testing recommendations for Chloromethyl Methyl Ether (CMME) can be found in Table 1.

#### IV. DATA SET SUMMARY AND EVALUATION

The key studies used in this assessment to fulfill the HPV requirements have been placed in an Endpoint-specific matrix, and further discussed below. Robust Summaries for each study referenced can be found in Section VII of this dossier.

##### A. Chemical/Physical Properties

All measurable HPV Endpoints for Chemical/Physical Properties have been completed (Table 2). At room temperature, CMME is a liquid with a vapor pressure of 286.6 hPa@25 C. Thus, a saturated atmosphere contains approximately 280,000 ppm CMME.

##### B. Environmental Fate and Biodegradation

All HPV Endpoints for Environmental Fate have been completed (Table 3). CMME is a very reactive molecule when dissolved in water (Table 2). The half-life of CMME in water is reportedly less than one second at 25°C and pH 7. At a concentration of <50% (limited details available) the half life was less than 2 minutes.

The level 3 Fugacity Model predicts essentially all CMME released in air will remain in air. The residence time would be 0.07 days. Thus CMME is rapidly degraded in air.

It is readily biodegradable in a MITI 1 biodegradation study.

##### C. Aquatic Toxicity

There is no aquatic toxicity data available for CMME (Table 4). As previously mentioned the rate of hydrolysis for CMME is extremely rapid with a half life at pH 7 and 25C of less than 1 second.

##### D. Mammalian Toxicity Endpoints

A summary of available toxicity data used to fulfill the HPV Endpoints for Mammalian Toxicity is found in Table 5. Each report has been further summarized in the Robust Summary section of this Dossier.

## 1.0 Acute Toxicity

The acute oral and dermal LD50s are 223 mg/kg and 300 mg/kg, respectively. The 7 hour LC50 is 55 ppm. The material is corrosive to the skin and eyes.

Thus based on the LD50 values, CMME would be considered moderate in toxicity. Due in part to the corrosive nature of CMME, protective equipment is required whenever contact with CMME is possible.

## 2.0 Repeated Dose Toxicity

A 30 day inhalation study was conducted at 1 and 10 ppm which demonstrated effects in the respiratory tract. At 10 ppm, approximately half of the CMME was degraded in the chamber.

In addition, carcinogenicity studies have been conducted in rats, mice and hamsters as well as epidemiology studies in humans. An increased incidence of pulmonary tumors was observed in mice exposed to CMME. The data is less conclusive for rats and hamsters. In a skin-painting study in mice, CMME acted as an initiator when followed by phorbol ester as the promotor. In several epidemiology studies, an increased incidence of lung cancer was observed in workers exposed to CMME.

## 3.0 Developmental Toxicity

There is no available developmental toxicity study (Table 6). Given the most likely route for human exposure is via the inhalation route and the rapid hydrolysis of CMME that would be expected to occur due to water present in the respiratory tract and blood stream, it is extremely unlikely that any CMME would reach a developing fetus. In addition, developmental toxicity data are available for each hydrolysis product. Thus no further testing for this endpoint is considered necessary.

## 4.0 Reproductive Toxicity

Since CMME is used as a closed system intermediate chemical, a reproduction study is unnecessary (Table 6). Given the most likely route for human exposure is via the inhalation route and the rapid hydrolysis of CMME that would be expected to occur due to water present in the respiratory tract and blood stream, it is extremely unlikely that any CMME would reach the reproductive organs. In addition, reproduction toxicity data are available for each hydrolysis product. Thus no further testing for this endpoint is considered necessary.

## 5.0 Mutagenicity and Chromosomal Aberrations

### 5.1 Mutagenicity Testing (Ames test)

There are two studies referenced in the literature which states that CMME was positive in the Ames test. Unfortunately, no additional information was provided and therefore they are rated a 4 in the Klimisch code.

### 5.2 - Chromosomal Aberrations

CMME was positive in the single in vitro study conducted and ambiguous in the single in vivo study conducted.

In conclusion, no further testing is considered necessary.

## V. REFERENCES

ACGIH TLV (2002). Threshold Limit Values for chemical substances and physical agents and Biological Exposure Indices. American Conference of Governmental Industrial Hygienists.

Drew, R.T., Laskin, S., Kuschner, M. and Nelson, N. (1975). Inhalation carcinogenicity of alpha halo ethers. Arch. Environ. Health 30:61-69.

Klimisch, H. J., Andreae, M. and Tillman, U. (1997). A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regul. Toxicol. Pharmacol. 25:1-5.

US EPA, (1998). Guidance for meeting the SIDS requirements (The SIDS Guide). Guidance for the HPV Challenge Program (11/31/98).

US EPA, (1999a). Determining the adequacy of existing data. Guidance for the HPV Challenge Program (2/10/99).

US EPA, (1999b). The use of structure-activity relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

## VI. ROBUST STUDY SUMMARIES -IUCLID

Data Sets are appended

Table 1. Test Plan Matrix for CHLOROMETHYL METHYL ETHER

	Info available?	OECD?	GLP?	Other study?	Estimated method?	Acceptable?
<b>PHYSICAL CHEMICAL</b>						
Melting Point	Y	R	R	N	N	Y, 2
Boiling Point	Y	R	R	N	N	Y, 2
Vapor Pressure	Y	R	R	N	N	Y, 2
Partition Coefficient	N	-	-	N	N	-
Water Solubility	N	-	-	N	N	-
<b>ENVIRONMENTAL FATE ENDPOINTS</b>						
Photodegradation	Y	N	N	N	Y	Y
Biodegradation	Y	Y	ND	N	N	Y
Transport between Environmental Compartmenats (Fugacity)	N	N	N	N	N	Y
Bioaccumulation	N	N	N	N	N	N
<b>ECOTOXICITY</b>						
Acute Toxicity to Fish	N	-	-	N	N	Y, data on degradation products
Acute Toxicity to Aquatic Invertebrates	N	-	-	N	N	Y, data on degradation products
Acute Toxicity to Aquatic Plants	N	-	-	N	N	Y, data on degradation products
<b>MAMMALIAN TOXICITY</b>						
Acute Toxicity	Y	N	N	N	N	Y
Repeated Dose Toxicity	Y	N	N	N	N	Y
Genetic Toxicity - Mutation (Ames)	Y	N	N	N	N	Y
Genetic Toxicity - Chromosomal Aberrations	Y	N	N	N	N	Y
Developmental Toxicity	N	-	-	-	N	Y, data on degradation products
Reproductive Toxicity	N	-	-	-	N	S, data on degradation products

Y = Yes; N = No; S = Supplemental, not required under HPV; - = Not applicable

**Table 2. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether  
Physicochemical Properties**

<b>Name (CAS No.)</b>	<b>Melting Point (°C)</b>	<b>Vapor Pressure (hPa @ 25°C)</b>	<b>Boiling Point (°C)</b>	<b>Partition Coefficient (log Kow)</b>	<b>Water Solubility (mg/L @ 20C)</b>
Chloromethyl methyl ether (CMME) (107-30-2)	-103.5 (measured)	162.7hPa@20C 286.6 hPa@25C (measured)	59 (measured)	-0.21 (estimated) not relevant since material is rapidly hydrolyzed	Not relevant since half life for hydrolysis is <1 second

**Table 3. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether  
Environmental Fate**

<b>Name (CAS No.)</b>	<b>Hydrolysis</b>	<b>Photodegradation Half life</b>	<b>Biodegradation</b>	<b>Environmental Transport Level III 1000 kg/hr released to air</b>
Chloromethyl methyl ether (CMME) (107-30-2)	Half life <1 second at 25C and pH 7	0.004 - 3.9 days	>80% in a MITI 1 study readily biodegradable	Air - 100.0% Water - 0.0000019% Soil - 0.042% Sediment - 0.0000000079% Residence time – 0.07 days

**Table 4. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether Ecotoxicity**

<b>Name (CAS No.)</b>	<b>Acute Fish 96-hour LC50 (mg/l)</b>	<b>Acute Invertebrate 48-hour EC50 (mg/l)</b>	<b>Algal 72-hour growth inhibition EC50 (mg/l)</b>
Chloromethyl methyl ether (CMME) (107-30-2)	<p align="center">No data</p> <p>Available data on hydrolysis products                      HCl - gambusia affinis - 282 mg/L                      Methanol - Lepomis macrochirus - 15,400 mg/L                      Formaldehyde - Ictalurus melas - 24.8 mg/L</p>	<p align="center">No data</p> <p>Available data on hydrolysis products                      HCL - Daphnia magna - 72 hr EC50 - 56 mg/L                      Methanol - Daphnia species - 10,000 mg/L                      Formaldehyde - Daphnia magna - 2 mg/L</p>	<p align="center">No data</p> <p>Available data on hydrolysis products                      HCl - Most likely unaffected at pH 5-10                      Methanol - Microcystis aeruginosa - 7 day EC0 - 530 mg/L                      Formadelhyde - Scenedesmus quadricauda - 8 day TGK - 2.5 mg/L</p>

**Table 5. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether  
Acute Toxicity**

<b>Name (CAS No.)</b>	<b>Acute Oral</b>	<b>Acute Dermal</b>	<b>Acute Inhalation</b>	<b>Dermal Irritation</b>	<b>Eye Irritation</b>	<b>Sensitization</b>
Chloromethyl methyl ether (CMME) (107-30-2)	≥223 mg/kg	300 mg/kg	55 ppm for 7 hour exposure	Corrosive	Corrosive	No data

**Table 6. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether Repeat-dose Toxicity**

<b>Name (CAS No.)</b>	<b>Repeat Dose</b>	<b>Carcinogenicity</b>	<b>Reproductive</b>	<b>Developmental</b>
Chloromethyl methyl ether (CMME) (107-30-2)	30 day study at 1 and 10 ppm	Positive in rats and humans	Unnecessary for closed system intermediates. Available data on hydrolysis products as found from most recent published dossiers HCl – NOAEL >50 ppm for changes in reproductive histopathology in 90 day inhalation study Methanol – NOAEL >1000 ppm in two generation rat reproduction study Formaldehyde – NOAEL 8.1 ppm for reproductive organs in 13 week inhalation study	No data Available data on hydrolysis products as found from most recent published dossiers HCl – NOAEL >50 ppm for changes in reproductive histopathology in 90 day inhalation study Methanol – NOAEL 1000 and 2000 ppm in rat and mouse developmental tox studies Formaldehyde – NOAEL >10 ppm in developmental tox study

**Table 7. Matrix of Available and Adequate Data on Chloromethyl Methyl Ether Genotoxicity**

<b>Name (CAS No.)</b>	<b>Genotoxicity (<i>in vitro</i> -bacterial)</b>	<b>Genotoxicity (<i>in vitro</i> - mammalian)</b>	<b>Genotoxicity (<i>in vivo</i>)</b>
Chloromethyl methyl ether (CMME) (107-30-2)	Positive based on limited data and results from animal bioassay	Positive in DNA chromosomal aberration test	Ambiguous in mouse micronucleus assay

**Table 8**  
**Test Plan Matrix for Chloromethyl Methyl Ether**

	CMME (107-30-2)
<b>PHYSICAL CHEMISTRY</b>	
Melting point, °C	-103.5 (measured) A
Boiling point, °C	59 (measured) A
Vapor Pressure, hPa at 25C	286.6 (measured) A
Water Solubility	Not relevant since half life for hydrolysis is <1 second NA
K <sub>ow</sub>	Not relevant since half life for hydrolysis is <1 second NA
<b>ENVIRONMENTAL FATE</b>	
Biodegradation	>80% in a MITI 1 study Readily biodegradable A
Hydrolysis	Half life <1 second at 25C and pH 7 A
Photodegradability	A
Transport between Environmental Compartments: ( <b>Fugacity Level III Model</b> ) Default assumption: 1000 kg/hr released into air, water, and soil.	
<b>ECOTOXICITY</b>	
Acute Toxicity to Fish (96hr LC50)	No data A due to rapid hydrolysis
Acute Toxicity to Aquatic Invertebrates (48hr EC50)	No data A due to rapid hydrolysis
Toxicity to Aquatic Plants (72hr EC50)	No data A due to rapid hydrolysis
<b>TOXICOLOGICAL DATA</b>	
Acute Toxicity (oral), mg/kg	≥223 mg/kg A
Acute Toxicity (dermal) mg/kg	300 mg/kg A

Acute Toxicity (inhalation)	55 ppm for 7 hour exposure A
Acute Eye Irritation	Corrosive A
Acute Skin Irritation	Corrosive A
Sensitization	No data NR
Repeated Dose Toxicity	30 day study A
Genetic Toxicity-Mutation	Positive A
Genetic Toxicity- Chromosomal Aberrations	Positive A
Toxicity to Reproduction	No data NR as a chemical intermediate
Developmental Toxicity	No data NA

<b>Legend</b>	
<b>Symbol</b>	<b>Description</b>
R	Endpoint requirement fulfilled using category approach, SAR
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties