

201-14982B

ROBUST SUMMARIES FOR
METHALLYL CHLORIDE, 3-CHLORO-2-METHYL-1-PROPENE

1. GENERAL INFORMATION

- 1.1. CAS NUMBER 563-47-3
1.2. CHEMICAL NAME 3-chloro-2-methyl-1-propene

2.0 PHYSICAL AND CHEMICAL DATA

2.1 MELTING POINT

- Test Substance: 3-chloro-2-methyl-1-propene, 99% purity
Method: OECD 102
GLP: Yes
Year: 2000
Results: < 0 °C
Data Quality: Code 1d
References: FMC Corporation, Princeton, NJ

2.2 BOILING POINT

- Test Substance: 3-chloro-2-methyl-1-propene, 99% purity
Method: OECD 103
GLP: Yes
Year: 2000
Results: 70 °C
Data Quality: Code 1a
References: FMC Corporation, Princeton, NJ

2.3 VAPOR PRESSURE

- Test Substance: 3-chloro-2-methyl-1-propene, 99% purity
Method: OECD 104
GLP: Yes

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Year: 2000
Results: 13.65 kPa @ 20 °C
static method
Data Quality: Code 1a
References: FMC Corporation, Princeton, NJ

2.4 PARTITION COEFFICIENT

Test Substance: 3-chloro-2-methyl-1-propene, 99% purity
Method: OECD 107
Temperature: 23 °C
GLP: Yes
Year: 2000
Results: 193
Flask-shaking method
Data Quality: Code 1a
References: FMC Corporation, Princeton, NJ

2.5 WATER SOLUBILITY

Test Substance: 3-chloro-2-methyl-1-propene
Method: OECD 105
Temperature: 25 °C
GLP: Yes
Year: 2000
Results: 180 mg/L
Data Quality: Code 1a
References: FMC Corporation, Princeton, NJ

3.0 ENVIRONMENTAL FATE AND PATHWAY

3.1 PHOTODEGRADATION

Test Substance: 3-chloro-2-methyl-1-propene

Method: Estimated by the AOP program (v. 1.90) which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.

GLP: No

Year: 2000

Results: For reaction with hydroxyl radicals, the predicted half-life is 3.2 hours with a rate constant of 3.96×10^{-13} cm³/molecule-sec.

Remarks: Code 2f

References: AOPWIN version 1.90, Syracuse Research Corporation, Syracuse, NY

3.2 STABILITY IN WATER (HYDROLYSIS)

Test Substance: 3-chloro-2-methyl-1-propene

Method: Estimated by HYDROWIN program (v. 1.67)

GLP: No

Year: 2000

Results: A rate constant could not be calculated by this program. Due to the high vapor pressure of methallyl chloride, it is not possible to test this compound in the laboratory. In the environment, methallyl chloride would volatilize rapidly and not be available for hydrolysis.

Remarks: The hydrolysis calculation by an acceptable method is assigned a reliability code of 2f.

References: HYDROWIN version 1.67, Syracuse Research Corporation, Syracuse, NY

3.3 TRANSPORT/DISTRIBUTION (FUGACITY MODEL)

Test Substance: 3-chloro-2-methyl-1-propene

Method: Estimated by EPI Suite Program (v.3.05)

Inputs: Molecular weight: 90.55
Henry's Law Constant: 0.0087 atm-m³/mole (Henry database)
Vapor Pressure: 102 mm Hg
Log Kow: 2.48 (calculated by model)
Soil Koc: 124 (calculated by model)

Year: 2001

GLP: No

Results:

Distribution using Level III Fugacity model

	Concentration	Half-Life	Emissions
	(percent)	(hr)	(kg/hr)
Air	5.67	5.23	1000
Water	66.1	360	1000
Soil	27.9	360	1000
Sediment	0.342	1.44e+003	0

Remarks:

Code 2f

References:

Syracuse Research Corporation, Syracuse NY

Description of EPI-WIN Fugacity Model (Help File Excerpt):

EPIWIN v3 contains a Level III fugacity model. The methodology and programming approach was developed by Dr. Donald Mackay and co-workers (Mackay et al., 1996a, 1996b; Mackay 1991). The model in EPIWIN v3 is a direct adaptation of this methodology and approach. While it uses the same equations as Mackay's EQC Level III Fugacity Model, it was adapted specifically for use in EPIWIN. It uses exactly the same default values as the Mackay model (Note: an executable version of Mackay's EQC model can be downloaded from The Environmental Modeling Centre (Trent University) Internet web-site: <http://www.trentu.ca/academic/aminss/envmodel/models.html>).

A detailed description of Level I, II and III fugacity models is not presented here; please see the Mackay publications and Internet web-site cited above. In general, fugacity models predict the partitioning of an organic compound in an evaluative environment. A Level III model does not assume an equilibrium state; it only assumes steady-state. The Level III model in EPI predicts partitioning between air, soil, sediment and water using various user-input parameters and/or inputs estimated by several EPI programs.

Note: all Fugacity Half-Life Values, Emission Values, Soil Koc and Advection Values have default values or estimation methods. User intervention is not required to generate model predictions. However, more accurate user-input data (e.g. measured half-life data) should result in better model predictions. Also, modification of various default values may be required for individual evaluations. A discussion of each "Fugacity" menu selection follows.

Half-Life Values

Half-lives are required for air, soil, sediment and water ... the fugacity cannot run without them.

If the half-lives in air, water, soil and sediment are known, the "Use Half-Lives Entered Below" should be selected and the known values should be entered in the appropriate fields. Often, however, this data is not available and requires estimation. The BIOWIN and AOPWIN programs are used to make these estimates. The AOPWIN air estimate is based upon estimated hydroxyl radical and ozone rate constants. AOPWIN does have an experimental database containing more than 700 compounds. If an entered structure has a database match, the database value is used instead of the program estimate.

The water, soil and sediment half-lives are based upon BIOWIN prediction times for either ultimate or primary biodegradation. The prediction times range from “Hours” to “Recalcitrant”. Each “time-range” has a default half-life value; these default values can be changed if desired. The default values were derived by Dr. Robert S. Boethling of the U.S. EPA based upon the methodology reported in the Boethling et al. (1994) journal article. The default values in EPI v3.02+ are slightly different than the default values in prior versions of EPI. If BIOWIN predicts “Weeks” for biodegradation, then a half-life of 15 days is applied to water and soil ... a half-life of 60 days is applied to sediment because the default “Half-Life Factor” for sediment is 4 times the value for water and soil (again, the default “Half-Life Factors” were derived by Dr. Robert S. Boethling). Each Biowin half-life is multiplied by the “Half-Life Factors”.

The Half-life entry box contains two buttons for “Set Biowin Half-life Values”. The “EPA default” button sets the values derived by Dr. Robert S. Boethling. The “Alternative” button sets slightly more conservative values.

Emission Values

The default Environmental Emission Rates are 1000 kg/hr to Air, Water and Soil (Sediment has a value of zero); these are the Mackay defaults. The Air, Water and Soil rates can be modified if desired.

EPIWIN can run the level III model once per EPI run using the emission rates shown (this is the program default) or multiple times per EPI run. Currently, “Multiple Level III Output” will run the Level III model 7 times using all permutations of Air, Water and Soil rates as either 0 or 1000 (the permutation where all rates are 0 is excluded).

Advection Values

The Advection Times apply to Air, Water and Sediment. These values should not be changed unless you are very familiar with the Mackay model. Access is available for advanced use only.

Soil Koc Value

The Fugacity Model requires a soil Koc value. By default, the Mackay Model calculates the soil Koc from the log Kow value. If desired, the soil Koc can be estimated by the PCKOCWIN program or directly entered by the user.

Other Input Parameters

The Fugacity Model cannot run without a vapor pressure. If the vapor pressure is not user-entered, the model uses the vapor pressure estimate by the MPBPWIN Program. If the MPBPWIN Program estimates a vapor pressure of zero (which can occur if an estimate is less than 1.00e-40 mm Hg), the fugacity model uses an assumed value of 1.00e-15 mm Hg (this value is low enough to have no sensitivity effect in the fugacity estimates). See section 5.3 concerning Henry’s law constant inputs. The model also requires a log Kow value. If the log Kow is not user-entered, the model uses the value from the KOWWIN Program (an experimental database value is used if available instead of the estimate).

The Fugacity model in EPIWIN has limited user-access to many parameters in the Mackay Level III Model. For example, parameters such as rain rate, aerosol deposition, soil water runoff, and diffusion mass transfer coefficients cannot be changed by the EPIWIN user. For these parameters, EPIWIN relies solely upon the defaults values as determined by Mackay and co-workers. This greatly simplifies application of a Level III model for most users. If you understand the inter-workings of a Level III model and need access to these parameters, you can download the Mackay EQC Model from the Internet web-site listed above.

3.4 BIODEGRADATION

Test Substance: 3-chloro-2-methyl-1-propene

Method: OECD guideline 301D

Test type: Closed bottle test

Contact time: 28 days

Inoculum: secondary clarifier supernatant from a wastewater treatment plant

Test conditions: Aerated mineral medium was dosed with 2 mg/L of methallyl chloride and approximately 0.5 mL of inoculum. Samples were kept at 20-22 °C and sampled 0, 7, 14, 21 and 28 days after treatment. The test contained two inoculum control groups, two phthalic acid reference groups and two treatment groups. Degradation was followed by the analysis of dissolved oxygen. The dissolved oxygen uptake of the test solution (corrected for uptake of blank inoculum) was expressed as a percentage of the theoretical oxygen demand of the test substance.

GLP: Yes

Year: 2001

Results: Methallyl chloride had degraded 71% by 28 days after treatment. See the following table for the amount of degradation over time.

Days After Treatment	Average Percent Degradation	
	Phthalic acid (reference substance)	Methallyl chloride
0	0	0
7	64	21
14	80	53
21	92	61
28	99	71

Remarks: Code 1a

References: Schaefer, E.C. and A.I. Siddiqui, "Methallyl Chloride: An Evaluation of Ready Biodegradability Using the Closed Bottle Test Method," Unpublished study for FMC Corporation, Agricultural Products Group, Princeton, NJ, 2002.

4.0 ECOTOXICOLOGY

4.1 ACUTE TOXICITY TO FISH

4.1.1 SOURCE #1

Test Substance: 3-chloro-2-methyl-1-propene, purity unknown

Method: APHA Standard Method No. 231

Species: Carassius auratus (fresh water)
Exposure Period: 24 hour
Type: Static
Analytical Monitoring: Yes
GLP: (Yes or No) No data
Year: 1971
Results: LC50 = 14 mg/l
Temperature 20 ± 1°C, pH = 7.8, open vessels with 6 fish in each
Data Quality: Code 4b
References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (Bridie, A.L., et al, "The acute toxicity of some petrochemicals to goldfish". Water Res. 13, 623-626, 1979)

4.1.2 SOURCE #2

Test Substance: 3-chloro-2-methyl-1-propene, purity unknown
Method: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15
Species: Leuciscus idus (fresh water)
Exposure Period: 48 hour
Type: Static
Analytical Monitoring: No
GLP: (Yes or No) No
Year: No data
Results: LC0 = 20 mg/l, LC50 = 22.5 mg/l, LC100 = 25 mg/l
Data Quality: Code 4b
References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (Huels AG Marl)

4.1.3 SOURCE #3

Test Substance: 3-chloro-2-methyl-1-propene, (96.38% purity)
Method: OECD Guideline for Testing of Chemical #203, Fish Toxicity Test (OECD , 1992)
Species: Rainbow trout, *Oncorhynchus mykiss*
Test Concentration (nominal): 6.3, 13, 25, 50 and 100 mg a.i./L

Exposure Period:	96 hours
Analytical Monitoring:	Yes
GLP:	Yes
Year:	Initiated 2000, experimental phase 2001
Results:	Empirically estimated to be > 100 mg a.i./L, the highest concentration tested. Due to the physical properties (high volatility) of methallyl chloride, an LC ₅₀ based on measured concentrations could not be obtained in an open exposure system. NOEC 50 mg a.i./L.
Remarks:	<p>The acute toxicity of Methallyl Chloride to the rainbow trout, <i>Oncorhynchus mykiss</i> was conducted for 96 hours from May 11 to May 15, 2001 at Springborn Laboratories, Inc., in Wareham, Massachusetts.</p> <p>The test was performed under static conditions at 14 ± 1°C with 5 concentrations of test substance and a dilution water control. The dilution water was characterized as having a total hardness and total alkalinity (as CaCO₃) of 40 and 37 mg/l respectively, a pH of 7.0 and a specific conductivity of 140 umhos/cm. Nominal concentrations of Methallyl Chloride were 0 mg/L (control), 6.3, 13, 25, 50 and 100 mg a.i./L. At 0-hour, measured concentrations ranged from 1.9 to 7.9 percent of the nominal fortified concentrations and were defined as 0.12, 0.99, 1.6, 3.8 and 7.9 mg/L. At 96-hour, the measured values for the 6.3, 13 and 25 mg a.i./L levels were below the limit of quantitation (0.0379 mg ai/l). Measured concentrations in the 50 and 100 mg ai/l treatment levels ranged from 0.091 to 0.10% of the nominal fortified levels and were defined as 0.045 and 0.10 mg ai/l respectively. Mean measured concentrations could <u>not</u> be used for the calculations. Based on the instability of the test substance any measured concentrations may not be indicative of rainbow trout exposure, due to the rapid volatilization of methallyl chloride from water.</p> <p>Organisms used in the test were obtained from a commercial supplier and acclimated to test conditions for at least 12 days at the contract laboratory. The photoperiod was 16 hours light and 8 hours darkness. Light intensity was approximately 70 to 80 footcandles. Ten rainbow trout were indiscriminately distributed to treatment and control aquaria. The test was performed in 20.8 -liter glass aquaria that contained 15 liters of test solution. Test vessels were randomly arranged in a water bath during the test. All animals were in good condition at the beginning of the study. Dissolved oxygen ranged from 6.4 to 9.9 mg/L during the study; pH ranged from 6.5 to 7.2 and temperature ranged from 13 to 14 °C.</p>
Data Quality:	Code 1
References:	Springborn Laboratories, Inc. Methallyl Chloride - Acute Toxicity to Rainbow trout (<i>Oncorhynchus mykiss</i>). Springborn Study Number 282.6143. FMC Study Number A2000-5260.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.2.1 SOURCE #1

Test Substance:	3-chloro-2-methyl-1-propene, purity unknown
Method:	Daphnien-Kurzzeitest, DIN 8412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse
Species:	Daphnia magna (Crustacea)
Exposure Period:	24 hour
Analytical Monitoring:	No
GLP: (Yes or No)	No
Year:	No data
Results:	EC50 = 7.2 mg/l Temperature 21°C; open vessels
Data Quality:	Code 4b
References:	IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (Huels AG Marl)

4.2.2 SOURCE #2

Test Substance:	3-chloro-2-methyl-1-propene, (96.38% purity)
Method:	OECD Guideline Reference Number 202
Species:	Daphnia magna
Exposure Period:	48 hours
Analytical Monitoring:	Yes
GLP:	Yes
Year:	2001
Results:	Based on nominal concentrations and the results of this study, the 48-hour EC ₅₀ was estimated by nonlinear interpolation to be 160 mg a.i./L (corresponding 95% confidence intervals calculated by binomial probability of 130 to 250 mg a.i./L). The No-Observed-Effect Concentration (NOEC) was determined to be 31 mg a.i./L. Due to the physical properties of methallyl chloride, an EC ₅₀ value based on measured concentrations for methallyl chloride and Daphnia magna could not be obtained in an open exposure system. Qualitatively, the

EC₅₀ lies between 50 and 250 mg a.i./L (nominal) in an open static system. Any measured concentrations were not indicative of exposure due to the rapid volatilization of methallyl chloride from water.

Remarks: The acute toxicity of methallyl chloride to the daphnid, *Daphnia magna*, was conducted for FMC Corporation for 48 hours from February 22 to 24, 2001 at Springborn Laboratories, Inc., in Marblehead, Massachusetts.

The test was performed under static conditions at 19 -20°C with five concentrations of test substance and a dilution water control. The dilution water was from the same source as the water used in the daphnid cultures and had a total hardness and alkalinity as CaCO₃ of 170 mg/l and 120 mg/l respectively, a pH of 7.9, and a specific conductivity of 500 umhos/cm. Nominal concentrations of methallyl chloride were 0 mg/L (control), 16, 31, 63, 130, and 250 mg/L.

Organisms used in the test were obtained from an in-house culture that was acclimated to test conditions. 5 daphnids were indiscriminately distributed to each of four replicates (A, B, C and D) of each treatment. The test was performed in 250 ml glass beakers that contained 200 ml of test solution. A 16 hour light and 8 hour dark photoperiod was automatically maintained with fluorescent lights that provide a light intensity of 80 to 100 foot candles. All animals were in good condition at the beginning of the study. One hundred percent survival occurred in the control.

Five different exposures were conducted with daphnia magna and methallyl chloride to establish an EC₅₀ based on immobilization. Qualitatively the EC₅₀ lies between 50 and 250 mg a.i./l (nominal). Due to limited solubility and the high volatility of methallyl chloride, it was not possible to establish an EC₅₀ based upon measured concentrations.

Data Quality: Code 1

References: Springborn Laboratories, Inc. Methallyl Chloride – Acute Toxicity to Daphnids, *Daphnia magna* Springborn Study Number 282.6144. FMC Study Number A2000-5261.

4.3 TOXICITY TO AQUATIC PLANTS

Test Substance: 3-chloro-2-methyl-1-propene, (96.38% purity)

Method: Following OPPTS Draft Guideline 850.5400, OECD Guideline #201 and EC Guideline Annex V - PART C.3

Species: *Pseudokirchneriella subcapitata*

Exposure Period: 96 hour

GLP: Yes

Year: 2001

Results:

Cell Density: The 96-hour EC₅₀ was calculated to be 160 mg a.i./L, with 95% confidence limits of 77 to 330 mg a.i./L. The 96-hour NoObserved-Effect Concentration (NOEC) was determined to be 42 mg a.i./L. These endpoints are based upon initial measured concentrations of methallyl chloride.

Biomass: The 72-hour EbC₅₀ was calculated to be 89 mg a.i./L, with 95% confidence limits of 32 to 240 mg a.i./L. Based on Kruskal-Wallis Test, the 72-hour NOEC was determined to be 210 mg a.i./L. Since 97% inhibition occurred at this treatment level, the NOEC was empirically estimated to be 24 mg a.i./L, the highest concentration tested with <10% inhibition of biomass

Growth Rate: The 72-hour ErC₅₀ was calculated to be 230 mg a.i./L, with 95% confidence limits of 180 to 280 mg a.i./L. Based on Williams Test, the 72-hour NOEC was determined to be <24 mg a.i./L. Since only 2.9% inhibition occurred at this treatment level, the NOEC was empirically estimated to be 24 mg a.i./L.

Based on the results of the algal recovery phase of this study, methallyl chloride was determined to have an algistatic, rather than algicidal effect on the growth of *Pseudokirchneriella subcapitata* at a nominal concentration of 1000 mg a.i./L.

Remarks:

The toxicity of methallyl chloride to the freshwater alga, *Pseudokirchneriella subcapitata*, was investigated. The test, which was designed to establish the 24, 48, 72 and 96 hour EC₅₀ values and the 96 hour no observed effect concentration (NOEC), was conducted from January 26 to February 5, 2001 (including the recovery phase) for FMC Corporation by Springborn Laboratories, Inc.

The test was conducted under static conditions with five concentrations of test substance and a dilution water control at 23 - 24°C. The dilution water was sterile enriched medium, adjusted to a pH of 7.5 ± 0.1 with hydrochloric acid or sodium hydroxide, if necessary, prior to use. The number of cells/mL was determined microscopically using a hemacytometer (Neubauer improved) and compound microscope every 24 hours during the exposure. Nominal concentrations of methallyl chloride were 0 mg/L (control), 64, 130, 250, 500 and 1000 mg/L. At 0 hour measured concentrations ranged from 33 – 41% of nominal concentration. The compound is highly volatile. Evaporation of the test substance from stock solutions and test solutions during preparation is suspected as the reason for measured concentrations being less than the nominal levels. At 96-hours of exposure, measured concentrations were below the limit of detection in all treatment levels tested. Based on the decline in test substance concentration, results are reported based on initial measured concentrations that defined the exposure concentrations as 24, 42, 100, 210 and 400 mg a.i./L.

Algae were distributed among three replicates of each treatment at the rate of approximately 1 x 10⁴ cells/mL. In order to estimate the impact that the presence of algal biomass had on the test substance concentration, an additional replicate flask of the 250 mg a.i./L (nominal) treatment level was prepared. This flask, which was not inoculated with algae, was analyzed at 96 hours of exposure for methallyl chloride concentration. The results of this analysis were compared with the results for the 250 mg a.i./L solution containing algae. Results demonstrated that the presence of algae was not responsible for the

decrease in test substance. Test vessels were 250 mL glass Erlenmeyer flasks that contained 100 mL of test solution. Test vessels were randomly arranged on a rotary shaker that was adjusted to 100 rpm and located in an incubator during the test. A 24 hour light 0 hour dark photoperiod was automatically maintained and provided a light intensity of 3200 to 5400 lux.

Recovery for algistatic/algicidal properties was measured. A composite sample of three replicate vessels was removed from the 1000 mg a.i./l test concentration. The sample was then diluted with freshly prepared medium to prepare a subculture with a nominal concentration of 64mg a.i./l. The performance of this subculture was used to determine if the effects of methallyl chloride was algistatic, in which case the cells would resume growth, or algicidal, in which case growth would not resume in the subculture

Data Quality:

Code 1

References:

Springborn Laboratories, Inc. Methallyl Chloride - Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata* Springborn Study Number 282.6145. FMC Study Number A2000-5262.

5.0 TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ORAL

Test Substance:

3-chloro-2-methyl-1-propene, clear liquid, 95.4% purity

Method:

40 CFR 163.81-1, United States EPA Acute Oral Toxicity Study

Species/strain:

Sprague-Dawley rats

Sex:

Male and Female

No. Animals/Group:

10/sex/dose, 4 dose levels

Post dosing observation period:

14 days

GLP: (Yes or No)

Yes

Year:

1982

Results:

The test material was administered as a 10% v/v solution in corn oil in a series of graded dose levels to groups of ten male and ten female fasted Sprague-Dawley rats. The rats were observed for signs of toxicity at 0.5, 1, 2, 3, 4 and 6 hours on the day of dosing and twice daily thereafter for thirteen days. On day 14 they were observed once. Animals dying intercurrently as well as animals surviving treatment and killed on day fourteen were necropsied.

The mortality data used to calculate the LC50 values and 95% confidence limits are summarized below:

Male: <u>Mean Dose Level (mg/kg)</u>	<u>Dead/Tested</u>
1639	9/10
1367	8/10
1183	7/10
1001	0/10

Female: <u>Mean Dose Level (mg/kg)</u>	<u>Dead/Tested</u>
1365	10/10
994	8/10
841	5/10
719	2/10

The LD50 values and 95% confidence limits are shown below:

Male: LD50 = 1149 mg/kg (982-1317 mg/kg)

Female: LD50 = 848 mg/kg (754-942 mg/kg)

The clinical signs generally observed at all dose levels included tremors, decrease locomotion, chromorhinorrhea, chromodacryorrhea, oral discharge, lacrimation, diarrhea, abdominogenital staining and ocular opacity. The rats began exhibiting signs within 30 minutes of dosing. By day 12 all surviving rats had returned to normal except for 4 incidences of ocular opacity. All deaths occurred by day 7 of the study. All surviving animals gained weight by the end of the study.

Internal lesions observed at necropsy in both animals which died during the study as well as those which were sacrificed at termination included gastric hemorrhages, occult blood in the intestines and fibrous adhesions between the stomach, the liver and the diaphragm. External signs correlated with those observed previous to death. The test material is classified as slightly toxic in both male and female rats, that is, the LD50 is greater than 500 mg/kg but less than 5000 mg/kg.

Data Quality:

Code 1a

References:

“Acute oral toxicity study in rats, Methallyl chloride”, FMC Toxicology Laboratory, Study Number I82-660.

5.1.2 DERMAL

Test Substance:

3-chloro-2-methyl-1-propene, clear liquid, 95.4% purity

Method:

40 CFR 163.81-2, United States EPA Acute Dermal Toxicity Study

Species/strain:	New Zealand White rabbits
No. Animals:	10
Dose:	2000 mg/kg
Vehicle:	Neat
Exposure Period:	24 hours
Post-exposure observations:	14 days
GLP: (Yes or No)	Yes
Year:	1982
Results:	<p>Ten New Zealand White rabbits were treated with the test material at a dose level of 2000 mg/kg. The test material was introduced under a gauze pad which was itself overlaid with impervious plastic sheeting. The test material was in contact with the clipped, abraded skin of the rabbits for twenty-four hours.</p> <p>The animals were observed for signs of toxicity at 0.5, 1, 2, 3, 4 and 6 hours on the day of dosing and twice daily thereafter for thirteen days. On day 14 they were observed once. Body weights were recorded on 0,7 and 14 days. Animals dying intercurrently as well as animals surviving treatment and killed on day 14 were necropsied.</p> <p>There were three deaths. A male rabbit died on day 10, one female rabbit died on day 2 and one female rabbit died on day 4. The rabbits appeared normal on the day of dosing, however, there were some vocalization and apparent discomfort. On day one all rabbits were either ataxic or had decreased locomotion. Nasal discharge, lacrimation and unthriftiness were also observed during the study. Most rabbits returned to normal by day 5 of the study.</p> <p>Erythema and edema were observed on all ten test sites during the study. Blanching and eschar were later observed on the test sites of all the surviving rabbits. There was a general loss of weight during the study (average male 0.49 kg, female 0.44 kg). At necropsy, local irritation (blanching, eschar) was observed on the test sites of all the surviving rabbits. This local irritation was judged to be test material related. Nasal discharge, lacrimation, oral discharge and consolidation of the lungs were also observed at necropsy.</p> <p>The dermal LD50 of the test material is judged to be greater than 2000 mg/kg in both male and female rabbits.</p>
Data Quality:	Code 1a
References:	“Acute dermal toxicity study, Methallyl chloride”, FMC Toxicology Laboratory, Study Number I82-659.
5.1.3 INHALATION	
Test Substance:	3-chloro-2-methyl-1-propene, clear liquid, purity undefined

Method:	Vapor
Type:	LC50
Species/strain:	Sprague-Dawley rats
Sex:	male and female
Exposure Period:	4 hr
Doses:	5 mg/liter
GLP: (Yes or No)	No
Year:	1982
Results:	<p>Five male and five female rats were exposed to the test compound or HEPA filtered room air (control) for 4 hr in 0.5 m³ inhalation chambers without access to food or water. The 4 hr exposure included the time of buildup to the test atmosphere conditions but not the chamber exhaust phase. After exposure, all rats were observed twice daily for 14 days for clinical signs of toxicity and any abnormal findings were recorded. Body weights were recorded immediately before exposure (day 1) and on days 2, 3, 4, 7 and 14. All animals were necropsied on day 15. Terminal body weights were collected on day 14. Gross examination included nasal passages, trachea, bronchi, lungs and other viscera. Lungs, liver, and kidneys were collected from each rat and preserved in 10% neutral buffered formalin.</p> <p>No deaths occurred during exposure and no toxic signs observed during the 14 days following exposure. Body weights of exposed males and females on study day 2 were less than at pre-exposure on day 1, whereas control rats gained weight. These changes were not statistically significant and not considered to be a significant toxicological response. There were no abnormal findings at necropsy. Male and female Sprague-Dawley rats given a single 4 hr exposure by inhalation at a nominal concentration of 6.3 mg/liter did not show any signs of toxicity through 14 days of observation.</p>
Data Quality:	Code 2e
References:	“Acute inhalation toxicity test in Sprague-Dawley rats using methallyl chloride”, Midwest Research Institute, FMC Study Number I82-661.

5.2 REPEATED DOSE TOXICITY

5.2.1 SOURCE #1

Test Substance:	3-chloro-2-methyl-1-propene, 90% purity
Species/strain:	Fischer 344 rats
No. Animals:	8 animals/dose
Sex:	Male

Dose:	75 and 150 mg/kg
Route of Administration:	Gavage
Control group:	Yes – corn oil
Exposure Period:	2 weeks
Frequency of Treatment:	5 days/week
Post-exposure observations:	Not done
GLP: (Yes or No)	No data
Year:	No data
Results:	Histopathologic examination of forestomachs from rats killed 24 hrs after the last dosing indicated that methallyl chloride in both doses caused a significant increase in the incidence and severity of mucosal cell proliferation and hyperkeratosis. The proliferative changes observed in the mucosa were more pronounced toward the proximal (esophageal) end of the forestomach with gradual diminution in severity in more distal aspects of the forestomach.
Data Quality:	Code 3a
References:	IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (Ghanayem, E. et al, Cancer Letters, 32:271-278, 1986).

5.2.2 SOURCE #2

Test Substance:	3-chloro-2-methyl-1-propene, 93% purity
Species/strain:	Fischer 344 rats
No. Animals:	10 animals/dose
Sex:	Male and female
Dose:	100, 316, 1000, 3160, 10,000 mg/kg in corn oil
Route of Administration:	Gavage
Exposure Period:	Single administration; observed 1 hr and 4 hr after dosing; once daily thereafter for 14 days
Frequency of Treatment:	Single administration
Method:	Groups of five rats of each sex were administered a single dose of 100, 316, 1000, 3160 or 10,000 mg/kg methallyl chloride in corn oil by gavage. Selection of doses was based on available data in the literature. The rats were observed daily and were killed 14 days after the dose was administered. A necropsy was performed on all animals.

GLP: (Yes or No) No data
Guideline: No
Year: 1978
Results: Rats that received 1000, 3160 or 10,000 mg/kg died before the end of the study. Final body weights were not recorded. Animals that died on day 1 frequently had darkened livers, spleens and kidneys, red lungs, and small intestines filled with red fluid. Animals that received 1000 mg/kg and died on day 2 or 3 frequently had tan livers, darkened lungs and thymus, and gas in the stomach. No compound-related effects were observed at necropsy in animals dosed at 100 or 316 m/kg.
Data Quality: Code 3b
References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.3 SOURCE #3

Test Substance: 3-chloro-2-methyl-1-propene, 93% purity
Species/strain: B6C3F₁ Mice
No. Animals: 10 animals/dose
Sex: Male and female
Dose: 31.6, 100, 316, 1000, 3160 mg/kg in corn oil
Route of Administration: Gavage
Exposure Period: Single administration; observed 1 hr and 4 hr after dosing; once daily thereafter for 14 days
Frequency of Treatment: Single administration
Method: Groups of five mice of each sex were administered a single dose of 31.6, 100, 316, 1000 or 3160 mg/kg methallyl chloride in corn oil by gavage. Selection of doses was based on available data in the literature. The mice were observed daily and were killed 14 days after the dose was administered. A necropsy was performed on all animals.
GLP: (Yes or No) No data
Guideline: No
Year: 1978
Results: All mice that received 3160 mg/kg died before the end of the study. Final body weights were not recorded. Yellow gelatinous intestines and pale livers, spleens and kidneys were found in mice that died before the

end of the study. No compound-related lesions were observed at necropsy in animals that survived to the end of the studies.

Data Quality: Code 3b

References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.4 SOURCE #4

Test Substance: 3-chloro-2-methyl-1-propene, 93% purity

Species/strain: Fischer 344 rats

No. Animals: 10 animals/dose

Sex: Male and female

Dose: 0, 89, 158, 281, 500, 750 mg/kg in corn oil

Route of Administration: Gavage

Control group: Yes – concurrent vehicle

Exposure Period: 14 consecutive days

Frequency of Treatment: Daily

Method: Groups of five rats of each sex were administered 0, 89, 158, 281, 500 or 750 mg/kg methallyl chloride in corn oil by gavage for 14 consecutive days. Animals were housed 5 per cage and received water and feed ad libitum. The rats were observed once per day and were weighed on days 1 and 15. A necropsy was performed on all animals.

GLP: (Yes or No) No data

Guideline: No

Year: 1978

Results: Rats that received 500 or 750 mg/kg of the test substance died before the end of the study. Male rats that received 281 mg/kg lost weight. Male rats that received 281 mg/kg lost weight. Final mean body weights of all other dosed groups and vehicle control rats were comparable. Animals that died during the study had dark stomachs, yellow intestines, pale and darkened areas on the liver, and/or dark fluid in the urinary bladder. The NOAEL was 158 mg/kg. The LOAEL was 281 mg/kg. Based on survival, 400 mg/kg was chosen as the highest dose for the 13-week studies.

Data Quality: Code 3b

References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.5 SOURCE #5

Test Substance: 3-chloro-2-methyl-1-propene, 93% purity

Species/strain: B6C3F₁ mice

No. Animals: 10 animals/dose

Sex: Male and female

Dose: 0, 125, 250, 500, 750, 1250, 1750, 2500 mg/kg in corn oil

Route of Administration: Gavage

Control group: Yes – concurrent vehicle

Exposure Period: 14 consecutive days

Frequency of Treatment: Daily

Method: Groups of five mice of each sex were administered 0, 125, 250, 500, 750, 1250, 1750 or 2500 mg/kg methallyl chloride in corn oil by gavage for 14 consecutive days. The 125 and 250 mg/kg groups of mice were started (without matched vehicle controls) 7 days after initiation of the studies because of the large number of deaths at 750 mg/kg. Animals were housed 5 per cage and received water and feed ad libitum. The rats were observed once per day and were weighed on days 1 and 15. A necropsy was performed on all animals.

GLP: (Yes or No) No data

Guideline: No

Year: 1978

Results: All mice that received 750, 1250, 1750 or 2500 mg/kg died on day 1. The death of 1/5 female mouse that received methallyl chloride at 250 mg/kg was considered unrelated to the chemical. Male and female vehicle control animals lost weight during the studies. Animals that died during the study had bright red or orange lungs, pale livers or soft intestines. No gross lesions were observed at necropsy at the end of the studies except for a pale liver in one male in the 125 mg/kg group.

Data Quality: Code 3b

References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.6 SOURCE #6

Test Substance:	3-chloro-2-methyl-1-propene, 93% purity
Species/strain:	Fischer 344 rats
No. Animals:	10 animals/sex/dose
Sex:	Male and female
Dose:	50, 100, 200, 300, 400 mg/kg in corn oil
Route of Administration:	Gavage
Control group:	Yes
Exposure Period:	13 weeks
Frequency of Treatment:	5 days/week
Method:	<p>Thirteen-week studies were conducted to evaluate the cumulative toxic effects of repeated administration of 3-chloro-2-methylpropene and to determine the doses to be used in the 2-year studies.</p> <p>Groups of 10 rats of each sex were administered 0, 50, 100, 200, 300 or 400 mg/kg methallyl chloride in corn oil by gavage, 5 days per week for 13 weeks. Animals were checked two times per day; moribund animals were killed. Clinical examinations were performed and animal weights were recorded once per week. At the end of the 13 week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized.</p>
GLP: (Yes or No)	No data
Guideline:	No
Year:	1978
Results:	<p>All rats that received methallyl chloride at 400 mg/kg and 5/10 males and 2/10 females that received 300 mg/kg died before the end of the studies. The deaths of 1/10 males that received 100 mg/kg and 2/10 females that received 200 mg/kg were considered to be due to gavage injury. Final mean body weights of male rats that received 200 or 300 mg/kg were depressed 5.0% and 6.6% relative to that of the vehicle controls. Compound-related clinical signs (primarily rough coats) were observed in 5/10 females that received 300 mg/kg and in 9/10 males and 4/10 females that received 400 mg/kg.</p> <p>Histologic evidence of chronic murine pneumonia was found in 5/10 male and 6/10 female vehicle controls. Kilham rat virus titers were found in 2/10 vehicle controls and Sendai virus titers in 3/10 vehicle controls.</p> <p>Focal areas of inflammation, which varied from acute to chronic, were observed in the livers of rats that received 300 and 400 mg/kg. The areas of necrosis were distributed throughout the liver. In the more</p>

acute lesions, the zone of necrosis was surrounded by congestion or neutrophils. The NOAEL was 100 mg/kg and LOAEL was 200 mg/kg.

Based on survival and incidence of liver lesions, methallyl chloride doses selected for rats for the 2-year studies were 0, 75 or 150 mg/kg in corn oil by gavage.

Data Quality: Code 3b

References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.7 SOURCE #7

Test Substance: 3-chloro-2-methyl-1-propene, 93% purity

Species/strain: B6C3F₁ mouse

No. Animals: 10 animals/sex/dose

Sex: Male and female

Dose: 0, 125, 250, 500, 750, 1250 mg/kg in corn oil

Route of Administration: Gavage

Control group: Yes – Corn Oil

Exposure Period: 13 weeks

Frequency of Treatment: 5 days/week

Method: Thirteen-week studies were conducted to evaluate the cumulative toxic effects of repeated administration of 3-chloro-2-methylpropene and to determine the doses to be used in the 2-year studies.

Groups of 10 mice of each sex received 0, 125, 250, 500 or 1250 mg/kg methallyl chloride in corn oil by gavage, 5 days per week for 13 weeks. Animals were checked two times per day; moribund animals were killed. Clinical examinations were performed and animals weights were recorded once per week. At the end of the 13 week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized.

GLP: (Yes or No) No data

Guideline: No

Year: 1978

Results: All mice that received methallyl chloride at 750 or 1250 mg/kg and 9/10 males and 5/10 females in the 500 mg/kg groups died before the end of the studies. The deaths of 1/10 male in the 500 mg/kg group and of mice in the other groups were considered to have been due to gavage injury. Compound-related

degenerative lesions were observed in the kidney and the liver. The kidney lesions consisted of degeneration and necrosis of cortical tubules, with accumulations of cellular debris in damaged tubules. Kidney lesions varied in severity within affected dose groups. The incidence and severity were greater in males than in females. Liver lesions consisted of coagulative necrosis and/or cytoplasmic vacuolization of hepatocytes. Liver and kidney lesions often occurred in the same mice; more severe lesions were often associated with the more severe kidney lesions. Some animals had neither lesions. Mice in all groups had lung lesions consisting of interstitial inflammation, sometimes with hyperplasia of bronchiolar epithelium and epithelialization of alveolar linings. The lesions were compatible with a viral infection. Mice in these studies had antibody titers for Sendai virus, PVM or mouse hepatitis virus. The NOAEL was 125 mg/kg and the LOAEL was 250 mg/kg.

Because of the liver lesions observed at 250 mg/kg, doses selected for mice for the 2-year studies were 0, 100 or 200 mg/kg methallyl chloride in corn oil by gavage.

Data Quality:

Code 3b

References:

IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (National Toxicology Program Technical Report No. 300, 1986).

5.2.8 SOURCE #8

Test Substance:

3-chloro-2-methyl-1-propene, 93% purity

Species/strain:

Rats/F344/N & Mice/B6C3F₁

No. Animals:

50 animals/species/sex/dose

Sex:

Male and female

Dose:

Rats – 0, 75, 150 mg/kg in corn oil

Mice – 0, 100, 200 mg/kg in corn oil

Route of Administration:

Gavage

Control group:

Yes – Corn Oil

Exposure Period:

103 weeks

Frequency of Treatment:

5 days/week

Method:

One hundred and three (103) -week studies were conducted to evaluate the cumulative toxic effects and carcinogenic potential of repeated administration of 3-chloro-2-methylpropene.

Groups of 50 rats of each sex received 0, 75, or 150 mg/kg methallyl chloride and 50 mice received 0, 100, or 200 mg/kg of methallyl chloride in corn oil by gavage, 5 days per week for 103 weeks. Animals were checked two times per day; moribund animals were killed. Clinical examinations were performed and

animals weights were recorded once per week. At the end of the 103 week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized.

GLP: (Yes or No)

No data

Guideline:

No

Year:

1980 - 1982

Results:

Mean body weights of high dose males was consistently 10% -15% below controls and late in the study experienced a marginal reduction in survival of high dose male rats. Mean body weights and survival in low dose male rats and in both dose groups of female rats were comparable with respective control groups. Mean body weights of high dose male mice and both female dose groups were slightly (5% - 9%) lower than controls. Survivability in both male and female mice was not affected by treatment.

Increased forestomach inflammation was not observed in rats, but was observed in male and female mice. Increased forestomach basal cell hyperplasia was observed in rats and mice of both sexes. Increased incidences of squamous cell papillomas were found in male rats, high dose female rats (150 mg/kg), and mice of both sexes. A slight increase of squamous cell carcinomas was detected in high dose male rats (150 mg/kg), but not in any female rat dose groups. Increased incidences of squamous cell carcinomas were found in mice of both sexes. No metastasis was seen in squamous cell carcinomas of the high dose male rats. The squamous cell carcinomas did metastasize to other organs in mice; two 100 mg/kg males, three 200 mg/kg males, and one 200 mg/kg female.

INCIDENCES OF FORESTOMACH LESIONS IN RATS AND MICE IN THE 2-YEAR GAVAGE STUDY

	INCREASED INFLAMMATION			BASAL CELL OR EPITHELIAL HYPERPLASIA			SQUAMOUS CELL PAPILLOMA			SQUAMOUS CELL CARCINOMA		
	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg
RATS	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg	0 mg/kg	75 mg/kg	150 mg/kg
Male	0/50	0/50	0/48	19/50	41/50	44/48	1/50	5/50	30/48	0/50	0/50	2/48
Female	0/50	0/50	0/50	24/50	42/50	45/50	1/50	1/50	10/50	0/50	0/50	0/50
MICE	0 mg/kg	100 mg/kg	200 mg/kg	0 mg/kg	100 mg/kg	200 mg/kg	0 mg/kg	100 mg/kg	200 mg/kg	0 mg/kg	100 mg/kg	200 mg/kg
Male	0/49	9/49	7/49	0/49	14/49	15/49	3/49	19/49	30/49	0/49	5/49	7/49
Female	2/50	3/48	9/44	4/50	6/48	13/44	0/50	15/48	29/44	0/50	1/48	2/44

Renal tubular cell adenocarcinomas (1/49) and transitional cell papillomas (1/46) of the urinary bladder were found in the 150 mg/kg male rats and renal tubular cell adenomas (1/50) and renal tubular cell adenocarcinomas (1/50) were observed in 75 mg/kg male rats.

Inflammation of the nasal cavity and of nephropathy/nephrosis were greater in the two dosed groups than in controls of rats and mice per sex.

There were lower incidences of adrenal gland pheochromocytomas and thyroid C-cell adenomas or combined carcinomas in all treated male rats. Negative trends were seen in hepatocellular adenomas or carcinomas in treated male mice and of hemangiomas or hemangiosarcomas in treated female mice.

Data Quality:

References:

Code 1b

National Toxicology Program Technical Report No. 300, 1986.

5.3 GENETIC TOXICITY IN VITRO

5.3.1 SOURCE #1

Test Substance:

3-chloro-2-methyl-1-propene, colorless liquid, 99.5% purity

Method:

Preincubation

Type:

Salmonella/Mammalian-Microsome Preincubation Mutagenicity Assay (Ames Test)

System of Testing:

S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538

Concentration:

16, 80, 400, 800 and 1000 ug with activation

5, 20, 100, 325, and 650 ug without activation

Metabolic Activation:

With and without

GLP: (Yes or No)

Yes

Year:

1984

Results:

Results of the preincubation assay were generated in two experiments. In the first experiment, the number of spontaneous revertants per plate for tester strain TA98 (with and without metabolic activation) was outside the acceptable range specified in the protocol. Therefore, TA98 was retested in a second experiment. In the first experiment, a 2.0 fold increase in TA1537 revertants per plate was observed in the presence of metabolic activation. In order to clarify this response, tester strain TA1537 was retested in the second experiment. In conclusion, methallyl chloride did not cause a positive response on any of the tester strains with or without metabolic activation by Aroclor induced rat liver microsomes, utilizing a sealed incubation chamber.

First Experiment:

With metabolic activation: Average revertants/concentration

Strain	Solvent DMSO	16 ug	80 ug	400 ug	800 ug	1600 ug
TA98	81	90	93	78	57	15
TA100	96	101	104	109	110	87
TA153	9	10	9	9	12	4
TA153	4	6	8	6	7	4
TA153	19	19	24	19	17	17

Without metabolic activation: Average revertants/concentration

Strain	Solvent DMSO	5 ug	20 ug	100 ug	325 ug	650 ug
TA98	67	68	105	72	61	22
TA100	101	94	83	100	95	92
TA1535	15	15	13	12	8	10
TA1537	6	3	3	5	5	4
TA1538	16	14	10	9	14	11

Second Experiment:

With metabolic activation

Strain	Solvent DMSO	16 ug	80 ug	400 ug	800 ug	1600 ug
TA98	27	24	27	22	24	16
TA1535	10	6	7	8	7	5

Without metabolic activation

Strain	Solvent DMSO	5 ug	20 ug	100 ug	325 ug	650 ug
TA98	14	18	17	14	15	16

Data Quality:

Code 1a

References:

“Salmonella/Mammalian-Microsome preincubation mutagenicity assay (Ames test),” Microbiological Associates, FMC Study Number A84-1329.

5.3.2 SOURCE #2

Test Substance: 3-chloro-2-methyl-1-propene, colorless liquid, >99 % purity

Method: EPA New and Revised Health Effects Guidelines, Office of Pesticides and Toxic Substances, Report No. EPA 560/6-82-001, October 1983.

Type: Sister chromatid exchange assay

System of Testing: Chinese hamster ovary (CHO) cells

Concentration: 8, 20, 40, 60 and 80 ug/ml with activation
25, 50, 75, 125 and 250 ug/ml without activation

Metabolic Activation: With and without

GLP: (Yes or No) Yes

Year: 1985

Results:

Statistical analysis of the data indicates a dose-related increase in SCE/metaphase frequency at dose levels of 50, 125 and 250 ug/ml without metabolic activation. The 250 ug/ml dose level without activation approximates a two-fold increase in SCE/metaphase frequency as compared to the untreated control. There were no statistically significant increases in SCE/metaphase at any dose levels with activation. Biological significance requires a two-fold increase in SCE frequency in at least one dose level as compared to the control and/or a significant dose-response pattern. Since the data meets these criteria, the statistically positive findings are deemed biologically significant. In conclusion, methallyl chloride is considered a weak inducer of sister chromatid exchanges at the dose levels tested.

Without Metabolic Activation

Compound	Dose (ug/ml)	No. Metaphases Scored	Range of SCE/ Metaphase	Total No. SCE's	Total No. Chromosomes	SCE/ Chromosome
Untreated	0	50	4-12	612	1000	0.612
DMSO	1 %	50	5-16	525	1000	0.525
MAC	25	50	1-25	697	1002	0.696
MAC	50	50	5-24	714	995	0.718
MAC	75	50	6-28	688	996	0.691
MAC	125	50	7-33	851	999	0.852
MAC	250	50	10-38	1067	1000	1.067

With Metabolic Activation

Compound	Dose (ug/ml)	No. Metaphases Scored	Range of SCE/ Metaphase	Total No. SCE's	Total No. Chromosomes	SCE/ Chromosome
Untreated	0	50	8-24	741	1000	0.741
DMSO	1 %	50	5-32	719	996	0.722
MAC	8	50	5-22	638	999	0.639
MAC	20	50	6-30	631	992	0.636
MAC	40	50	5-22	710	999	0.711
MAC	60	50	8-27	768	1000	0.768
MAC	80	50	5-27	794	999	0.795

Data Quality:

1a

References:

Pharmakon Research International Inc, FMC Study Number A85-1606.

5.4 GENETIC TOXICITY IN VIVO

Test Substance:

3-chloro-2-methyl-1-propene

Method:

OECD Guideline 474

Type:

Micronucleus assay

Species/strain:

NMRI mouse

Sex:

Male and female

Route of Administration:

Gavage

Exposure Period:

Single application

Doses:

501 mg/kg (male); 631 mg/kg (female)

GLP: (Yes or No)

Yes

Year:

1983

Results:

Methylal chloride administered at the maximum tolerable dose did not show any clastogenic activity at 24, 48 or 72 hrs post application.

Data Quality:

Code 2a

References: IUCLID Data Sheet for 3-chloro-2-methylpropene, CAS No. 563-47-3, October 23, 1995 (Huels AG Marl Report No. MK 90/0004, 1991, unpublished)

5.5 COMBINED REPEATED DOSE WITH REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING

Test Substance: Methallyl chloride, 94.8% purity

Species/strain: Wistar rats

No. Animals: Six groups –
Main groups: 20 rats (10 male and 10 female)
Recovery groups: 10 rats (5 male and 5 female); Control recovery and high dose recovery

Sex: Male and female

Dose: 0, 20, 60, 180 mg/kg in corn oil

Route of Administration: Gavage

Control group: Yes

Exposure Period: 54 days

Frequency of Treatment: Daily

Method: The test material was dissolved in corn oil and administered daily via oral gavage at doses of 20, 60 and 180 mg/kg/bw/day. A concurrent control group and control recovery group received corn oil. There were 10 male and 10 female rats per group and the recovery groups consisted of 5 male and 5 female rats per group. The prepared test material solution was administered at appropriate doses to specific groups prior to the mating period, during mating period and during post-mating period (in males), during pregnancy and up to lactation day 4 (in females). In the control recovery and high dose (recovery) groups the treatment period was followed by a 14-day no treatment (recovery) period. The recovery period of the study started from the day of sacrifice of the first littered animals. The prepared test solutions were determined analytically for active ingredient at two times (day-0 of treatment and in the 2nd month of the treatment period). The stability and homogeneity of the test item solution was confirmed prior to the start of the treatment and the prepared solution was administered within the stability period.

Animals from all the groups were observed for clinical signs, physical abnormalities, changes in body weight, food consumption and survival. The functional observation battery was done shortly before sacrifice for 5 male and 5 females randomly selected from each group. For recovery groups functional observation was conducted along with the main groups. Hematology and clinical chemistry were performed for 5 males and 5 females randomly selected from each group at the end of the pre-mating period and recovery period. Histopathological examination of all the tissues from the randomly selected 5 males and 5 females from control and high dose groups was carried out. The data was statistically analyzed.

GLP: (Yes or No) Yes

Guideline: OECD 422

Year: 2002

Results: Concentrations of 20 and 60 mg/kg/day did not have any adverse effects on general health, body weight, food consumption, hematological and biochemical parameters and reproductive performance of dams and sires.

At 180 mg/kg, no treatment-related effects were seen on general health, body weights, food consumption and hematological parameters. Treatment caused effects on total bilirubin and liver enzymes in females, increased the post-implantation loss and thereby decreasing the number of live pups at birth. Histopathological examination revealed treatment-related epithelial hyperplasia in non-glandular stomach in both sexes.

Under the conditions of the study, the No Observed Adverse Effect Level (NOAEL) was determined to be 60 mg/kg/day.

Data Quality: Code 1a

References: Krishnappa, H. "Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test by gavage with methallyl chloride RAL 129 in wistar rats", Rallis Research Centre, FMC Study A1999-5052, May 18, 2002, unpublished.

CRITERIA FOR RELIABILITY CODES

(Adapted from Klimisch et al 1997)

<u>Code of Reliability</u>	<u>Category or reliability</u>
1	Reliable without restriction
1a	GLP guideline study (OECD, EC, EPA, FDA, etc.)
1b	Comparable to guideline study
1c	Test procedure in accordance with generally accepted scientific standards and described in sufficient detail
2	Reliable with restrictions
2a	Guideline study without detailed documentation
2b	Guideline study with acceptable restrictions
2c	Comparable to guideline study with acceptable restrictions
2d	Test procedure in accordance with national standard methods with acceptable restrictions
2e	Study well documented, meets generally accepted scientific principles, acceptable for assessment
2f	Accepted calculation method
2g	Data from handbook or collection of data
3	Not reliable
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system
4	Not assignable
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference not yet translated
4e	Documentation insufficient for assessment