National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Probit function technical support document

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substance name	CAS number
Methyl chloroformate	**79-22-1**

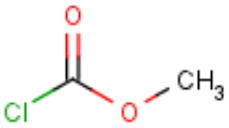
This document describes the derivation of a probit function for application in a quantitative risk analysis (QRA). The probit function has been derived according to the methodology described in RIVM report 2015-0102.

This document has been checked for completeness by the Netherlands' National Institute of Public Health and the Environment (RIVM). The contents of this document, including the probit function, has been approved by the Dutch Expert Panel on Probit Functions on scientific grounds. External parties have had the opportunity to comment on the derivation of the proposed probit function. The status of this document has now been raised to "inhoudelijk vastgesteld" (approved content).

Detailed information on the procedures for the derivation, evaluation and formalization of probit functions is available at http://www.rivm.nl/en/Topics/P/Probit_functions.

Technical support document Methyl chloroformate

1. Substance identification



CAS-number:	79-22-1
IUPAC name:	Methyl chloroformate
Synonyms:	Carbonochloridic acid, methylethyl ester; chlorocarbonic acid, methylethyl ester; chloroformic acid methyl ester; formic acid, chloro-, methyl ester; methyl chlorocarbonate
Molecular formula:	$C_2H_3ClO_2$
Molecular weight:	94.5 g/mol
Physical state:	liquid (at 20°C and 101.3 kPa)
Boiling point:	71°C (at 101.3 kPa)
Vapour pressure:	13.7 kPa (at 20°C)
Saturated vapor conc:	137000 ppm = 539000 mg/m^3 (at 20°C)
Conversion factor:	1 mg/m^3 = 0.254 ppm (at 20°C and 101.3 kPa)
	1 ppm = 3.931 mg/m^3 (at 20°C and 101.3 kPa)
Labelling:	Human H: 302-330-312-314

2. Mechanism of action and toxicological effects following acute exposure

Acute effects: Methyl chloroformate is an irritant and corrosive; the health endpoints are all related to these properties. The main target organs and tissues for airborne exposure to methyl chloroformate are the cornea, conjunctiva, skin and respiratory tract. Methyl chloroformate hydrolyses rapidly in water at room temperature but is not expected to hydrolyse rapidly in ambient air. Symptoms of high exposure are laboured breathing, secretions from nose, mouth and eyes and prostration.

Damage in the upper respiratory system results in mucus secretion and laryngospasm. In addition, pulmonary oedema has been described in animals. The resulting hypoxemia will cause CNS and cardiovascular (myocardial ischemia) effects. Lethality results when the respiratory damage proceeds to inflammation, degeneration and necrosis of affected tissue, atelectasis, emphysema and finally death.

Long-term effects: Chronic exposure produces essentially the same type of health effects. Reactive Airways Dysfunction Syndrome, an acquired asthma-like condition, is a possible consequence after single high exposure to methyl chloroformate. Symptoms occur within minutes to hours after the initial exposure and may persist as non-specific bronchial hyperresponsiveness for months to years.

3. Human toxicity data

No informative reports on human toxicity following acute inhalation exposure were identified in which details about both lethal or non-lethal health effects and the exposure have been documented in sufficient detail.

4. Animal acute toxicity data

During the literature search the following technical support documents and databases were consulted:

1. AEGL final TSD, ERPG document and EU RAR and reference database for methyl chloroformate, covering references before and including 1995.

2. An additional search covering publications from 1980 onwards was performed in HSDB, MEDline/PubMed, Toxcenter, IUCLID, ECHA, RTECS, IRIS and ToxNet with the following search terms:
   - Substance name and synonyms
   - CAS number
   - lethal*
   - mortal*
   - fatal*
   - LC_{50}, LC
   - probit
3. Unpublished data were sought through networks of toxicological scientists.

Animal lethal toxicity data focused on acute exposure are described in Appendix 1. A total of 11 studies were identified -with 11 datasets for 2 species- with data on lethality following acute inhalation exposure. No datasets were assigned status A for deriving the human probit function, 2 datasets were assigned status B and 9 were assessed to be unfit (status C) for human probit function derivation.

Sensory irritation

A total of 1 study was identified in which sensory irritation was studied. In this study the following RD_{50} value was observed:

Table 1 *Sensory irritation data for methyl chloroformate*

Species/strain	RD_{50} (mg/m^3)	Exposure duration (min)	Author/year
Swiss-Webster mice	206^{NS}	30	Carpenter 1982

NS: not specified if a plateau in response was reached.

5. Probit functions from individual studies

All available acute lethality data on methyl chloroformate are displayed in

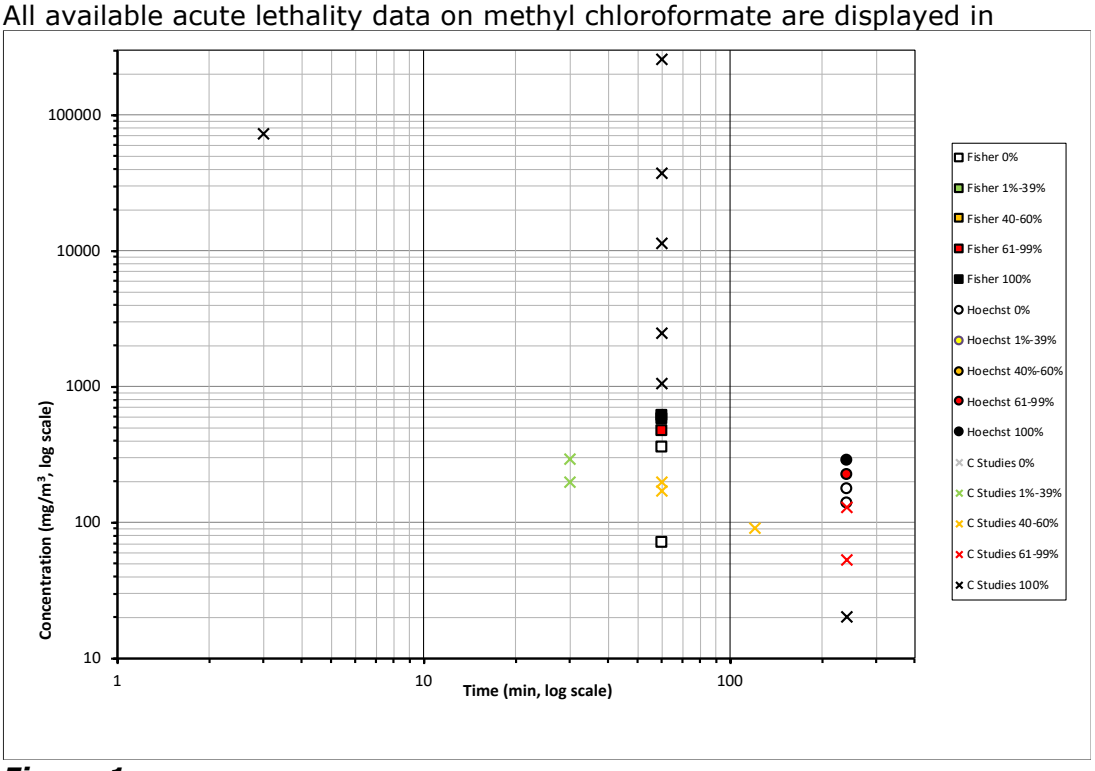


Figure 1.

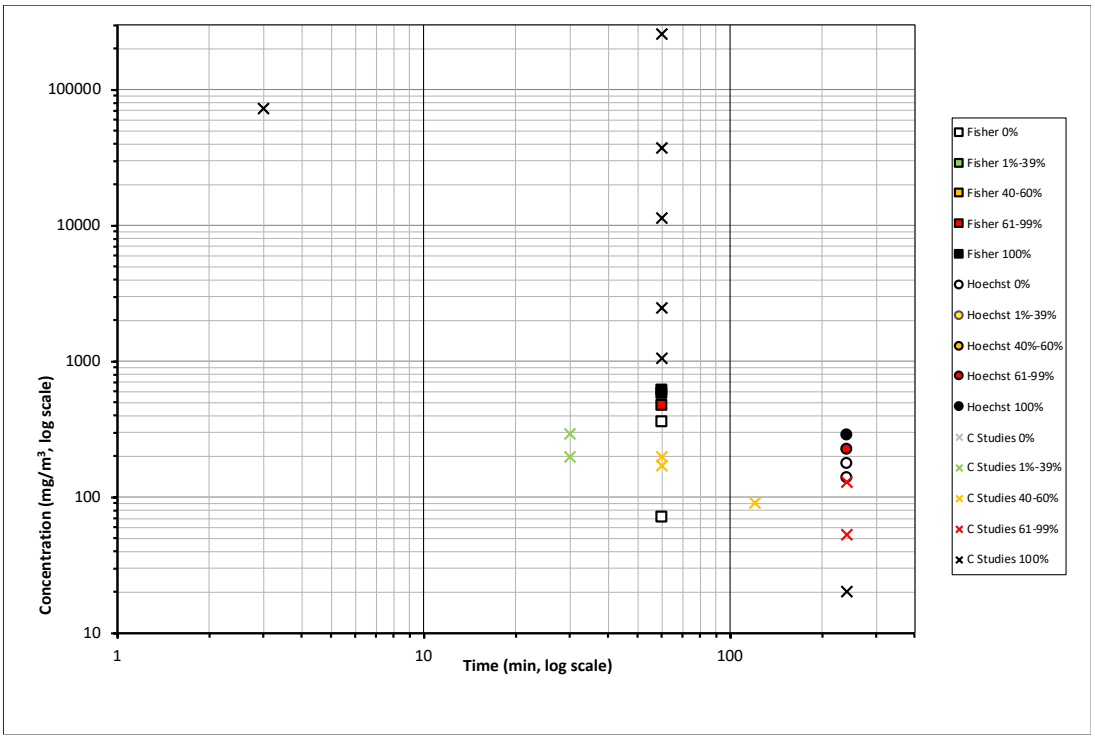


Figure 1 *All available acute lethality data for methyl chloroformate.*

The data that were selected for initial analysis of the animal probit function are presented in Table 2 and

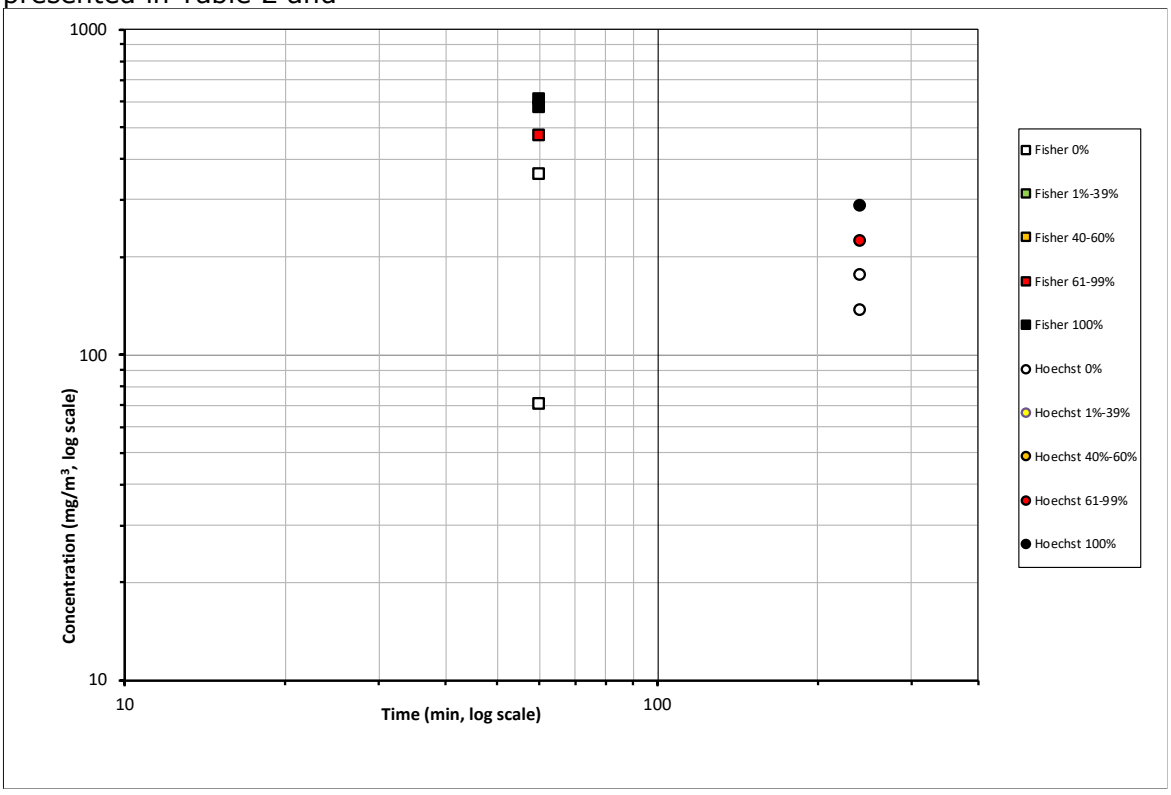


Figure 2. Both B1 studies were initially selected for derivation of the animal probit function for methyl chloroformate.

It was possible to derive a probit function for methyl chloroformate based on the available studies with B1 quality.

Probit functions have been calculated and reported in Appendix 1 for each of the reported studies. The results of the calculations are presented in Table 2. The time extrapolation was made with the default n-value of 2.

Table 2 *Data selected for initial analysis of the animal probit function of methyl chloroformate.*

Study ID	Species	Probit (C in mg/m^3, t in min)	LC_{50} at tested exposure duration (mg/m^3) 95% C.I.	LC_{50}, 30 minutes (mg/m^3) 95% C.I. *(underline italic for scaled values)*	n-value 95% C.I.
B1.1	Rat	*60-min LC_{50}*	452 (416 – 483)	*639*	N/A
B1.2	Rat	*240-min LC_{50}*	209 (196 - 224)	*591*	N/A

The data of the 2 B1 studies with rats are presented graphically below.

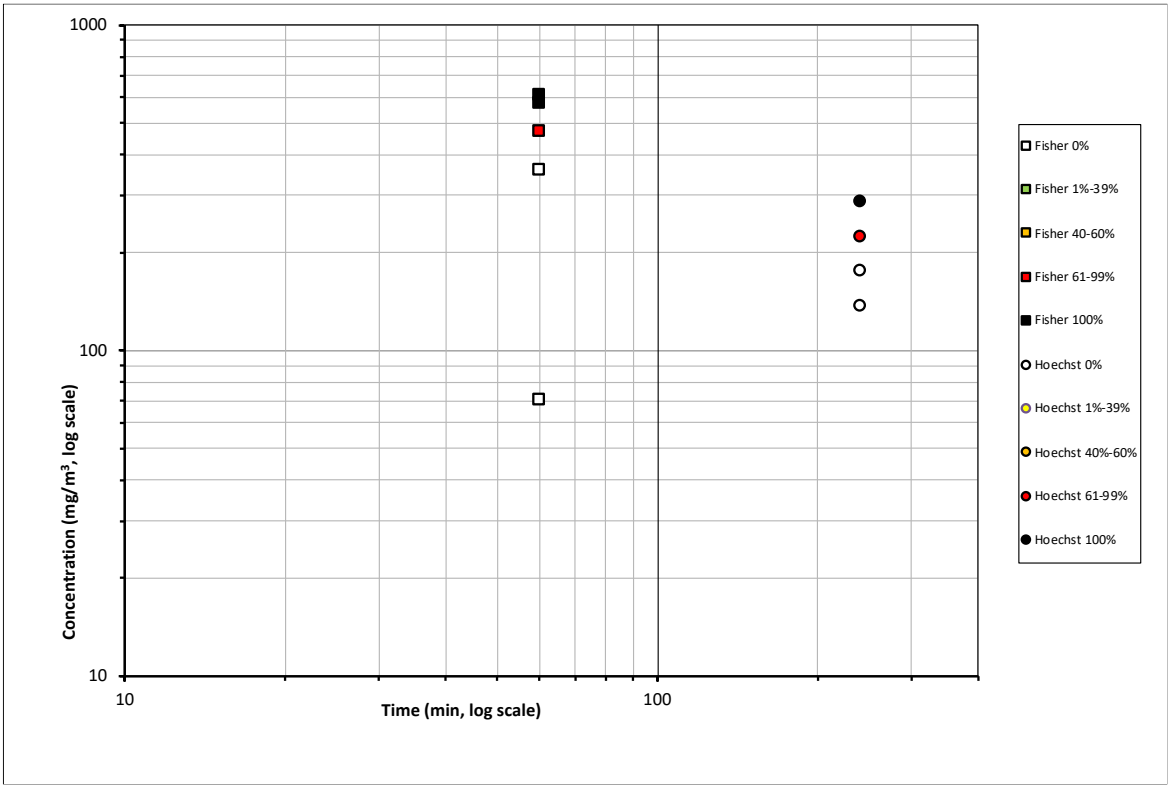


Figure 2 *Data selected for the initial analysis for the derivation of the animal probit function of methyl chloroformate.*

Based on criteria outlined in the guideline, the data from study B1.1 were selected for the final dataset for the derivation of the animal probit function. These 60-min data were preferred over the 240-min data from study B1.2 because they align better with the preferred exposure duration of 30-60 minutes.

The data that were selected for final analysis of the animal probit function are presented in Table 3 and Figure 3. The final data eligible for calculating the animal probit function contains one dataset from one study and includes data from one animal species.

Table 3 *Data selected for the derivation of the animal probit function of methyl chloroformate.*

Study ID	Species	Probit (C in mg/m^3, t in min)	LC_{50} at tested exposure duration (mg/m^3) 95% C.I.	LC_{50}, 30 minutes (mg/m^3) 95% C.I. *(underline italic for scaled values)*	n-value 95% C.I.
B1.1	Rat	*60-min LC_{50}*	452 (416 – 483)	639	N/A

The data of the selected dataset is presented graphically below.

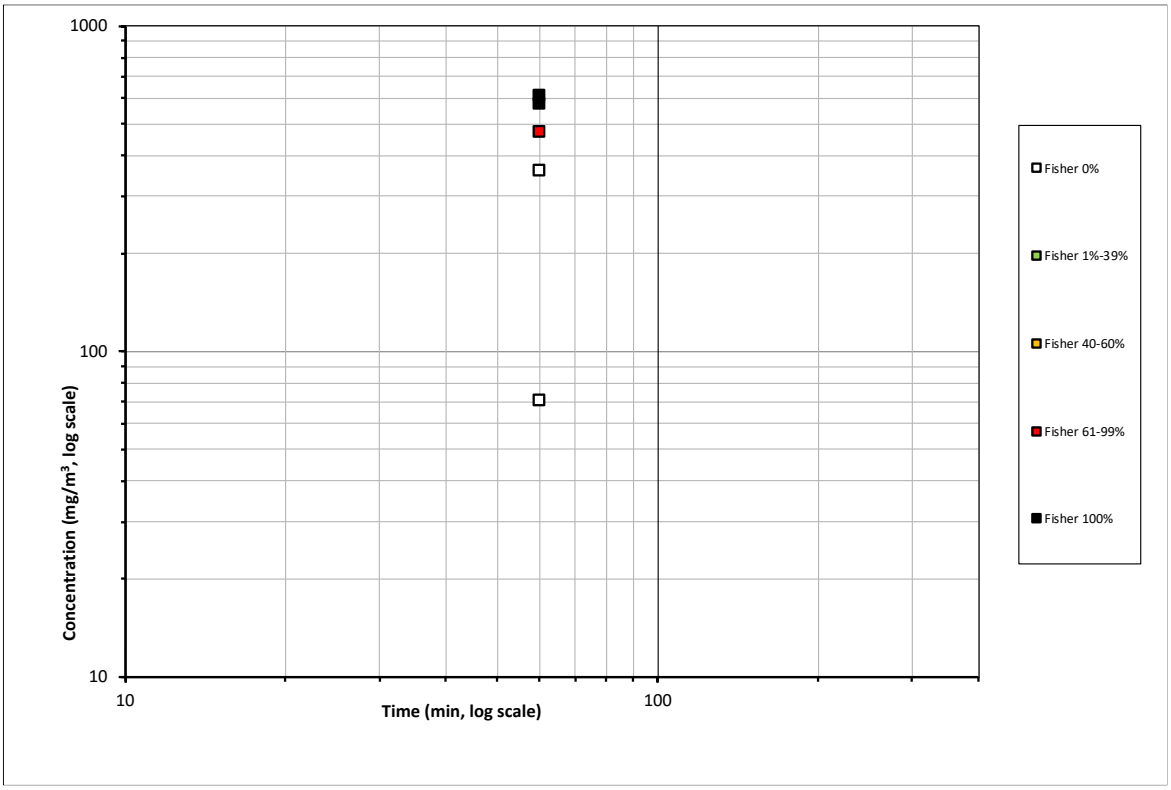


Figure 3 *Final data selected for derivation of the animal probit function of methyl chloroformate.*

6. Derivation of the human probit function

To derive the human probit function the results from Study B1.1 have been used to derive a point of departure as outlined above. There are no A-quality studies available, and study B1.1 fits the preferred exposure duration of 30-60 minutes better than the 240-minute data from study B1.2. Study B1.2 is used as supportive evidence.

The Point of Departure for the human probit function is a 60-minute rat LC_{50} value of 452 mg/m^3 and the default n-value of 2.

The human equivalent LC_{50} was calculated by applying the following assessment factors:

Table 4 Rationale for the applied assessment factors.

Assessment factor for:	Factor	Rationale
Animal to human extrapolation:	3	No rationale to deviate from the default assessment factor
Nominal concentration	1	In the applied B1 study analytical concentrations were reported
Adequacy of database:	1	The database is relatively strong with 2 well conducted B1-studies and does not justify an assessment factor >1

The estimated human equivalent 60-minute LC_{50} value is 452 / 3 = **151 mg/m³**.

No reliable experimentally determined n-value was available, so the default n-value of **2.0** was used. Assuming a regression coefficient (b×n) of 2 for the slope of the curve, the b-value can be calculated as 2 / n = **1.0**.

The human probit function is then calculated on the human equivalent 60 min LC_{50} using the above parameters to solve the following equation to obtain the a-value (the intercept): $5 = a + 1 \times \ln (151^2 \times 60)$ resulting in the a-value of **-9.124**.

Pr = -9.12 + 1 × ln (C^2 × t) with C in mg/m³ and t in min.

The derived human probit function has a scientifically weak basis. The probit function is based on 1 study in the rat with B quality (but supported by another B quality study), with 5 groups of 10 animals and lethality ranging from 0-100%.

The calculated human 60 min $LC_{0.1}$ (Pr = 1.91) calculated with this probit equation is 32 mg/m³ and the calculated human 60 min LC_1 (Pr = 2.67) is 47 mg/m³.

Table 5 *LC-values calculated with the derived probit function compared with existing acute inhalation exposure guidelines.*

Estimated level	30 min (mg/m³)	60 min (mg/m³)
0.1% lethality, this probit	45	32
1% lethality, this probit	66	47
AEGL-3 (2016, final)	33	26
ERPG-3 (2017)		20
LBW (2015)	33	26

Compared with equivalent (inter)national guideline levels as presented in the table above, the lethal levels derived with this probit function are comparable.

Appendix 1 Animal experimental research

Study ID: B1.1

Author, year: **Fisher 1981**
Substance: methyl chloroformate
Species, strain, sex: Male and female Fischer 344 (Charles River) rats
Number/sex/conc. group: 5 rats/sex/concentration
Age and weight: 50-60 days at exposure, males 156-204 gr., females 114-149 gr.
Observation period: 10 days

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*No GLP statement provided. Laboratory quality statement provided*
Study carried out according to OECD 403 guideline(s)	*OECD guideline 403 did not exist at the time. Most OECD 403 criteria appear to be met*
Stability of test compound in test atmosphere	*No mention of aerosol formation / condensation, but unlikely given the atmosphere generation method and concentration range*
Use of vehicle (other than air)	*HEPA filtered air*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body in a 1.3 m^3 Hinner-style chamber*
Type of restrainer	*N/A*
Pressure distribution	*1 mm H_2O negative pressure*
Homogeneity of test atmosphere in breathing zone of animals	*Test atmosphere was generated by evaporation and diluted with air before introduction into the chamber.*
Number of air changes per hour	*In excess of 12 air changes/h, typically 16 ft^3/min = 435 l/min = 21 air changes/h*
Equilibration time (t95)	*Estimated to be 9 minutes*
Start of exposure relative to equilibration	*At start of concentration build-up, animals remained inside the chamber until the concentration had returned to zero*
Actual concentration measurement	*Concentrations were monitored using real-time variable pathlength infrared photo-spectrometry. Sampling in the centre of the exposure chamber, after verifying an even (<4% variability) concentration distribution*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*Presence or absence of aerosol not reported*
Assessment of Reliability	***B1*** *Only one exposure duration, otherwise well conducted and described study*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Measured	Adjusted		Male	Female
Rat	0		60	0/5	0/5
	71		60	0/5	0/5
	361		60	0/5	0/5
	475		60	5/5	2/5
	579		60	5/5	5/5
	610		60	5/5	5/5

The authors reported the following concentrations: nominal concentrations, the concentrations after steady state was reached and the time-weighted average concentrations. The table lists the time-weighted average concentration. Actual exposure was 71% - 93% of nominal.
Reduced respiratory rate, dyspnea and gasping were reported in animals exposed to concentrations of 361 mg/m^3 and above. 23/27 deaths occurred within 4 days post exposure.

Probit function
The probit function and associated LC-values have been calculated using the DoseResp program (Wil ten Berge, 2016) as
$Pr = a + b \times lnC + d \times S$
with C for concentration in mg/m^3 and S for sex (0 = female, 1 = male).

Probit function	Species	a	b	d
Sex as variable	Rat	-73.8	12.7	1.93
Sexes combined	Rat	-58.3	10.4	

The LC_{50} values for both sexes did not differ by more than a factor of 2. This does not support the proposition that sex differences exist in the lethal response. For this reason, the data from both sexes were pooled and analysed to derive the animal probit function.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. Male	LC_{50} (mg/m^3) 95%-C.I. Female	LC_{50} (mg/m^3) 95%-C.I. Combined
60	416 (378 - 456)	484 (443 – 522)	452 (416 – 483)

No C × t probit function could be calculated from these data alone.

Study ID: B1.2

Author, year: **Hoechst 1986**
Substance: methyl chloroformate
Species, strain, sex: male and female Hoe: WISKf (SPF71) rats
Number/sex/conc. group: 5 / sex / concentration
Age and weight: 8-10 weeks, males 161-198 gr., females 164-194 gr
Observation period: 14 days

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*GLP statement provided*
Study carried out according to OECD 403 guideline(s)	*Compliance with OECD guideline 403 stated*
Stability of test compound in test atmosphere	*No aerosol formation / condensation or hydrolysis reported*
Use of vehicle (other than air)	*Air*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution	*Chamber pressure was 0.8 mbar below atmospheric pressure*
Homogeneity of test atmosphere in breathing zone of animals	*Test substance was continuously fed to a vaporizer head and evaporated at 72 °C*
Number of air changes per hour	*6-12 m^3/h in a 2.25 m^3 chamber, which equals 2.67-5.33 air changes/h*
Equilibration time (t95)	*t95 = stated to be 2-4 minutes*
Start of exposure relative to equilibration	*Probably after complete equilibration, but not explicitly stated*
Actual concentration measurement	*Infrared photo-spectrometry of 'respiratory air' every 15 min. Additional two samples per exposure period for analytical chemistry (method not specified, probably chromatography)*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*Presence or absence of aerosol not reported*
Assessment of Reliability	***B1*** *Only one exposure duration, otherwise well conducted and described study*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Measured	Adjusted		Male	Female
Rat	138		240	0/5	0/5
	177		240	0/5	0/5
	224		240	5/5	3/5
	287		240	5/5	5/5

Probit function

The probit function and associated LC-values have been calculated using the DoseResp program (Wil ten Berge, 2016) as

$Pr = a + b \times lnC + d \times S$

with C for concentration in mg/m^3, t for time in minutes and S for sex (0 = female, 1 = male).

Probit function	Species	a	b	d
Sex as variable	Rat	-60.0	12.1	1.13
Sexes combined	Rat	-54.3	11.1	

The LC_{50} values for both sexes did not differ by more than a factor of 2. This does not support the proposition that sex differences exist in the lethal response. For this reason, the data from both sexes were pooled and analysed to derive the animal probit function.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. Male	LC_{50} (mg/m^3) 95%-C.I. Female	LC_{50} (mg/m^3) 95%-C.I. Combined
240	199 (183 - 217)	219 (201 – 239)	209 (196 - 224)

No C × t probit function could be calculated from these data alone. The authors graphed a 240-min LC_{50} of 200 mg/m^3 for males and 208 mg/m^3 for females.

Study ID: C.1

Author, year: ***Bio-Test 1975***
Substance: methyl chloroformate
Species, strain, sex: Charles River rats, male and female
Number/sex/conc. group: 10 per sex per concentration
Age and weight: unspecified
Observation period: 14 days

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*GLP did not exist at the time*
Study carried out according to guideline(s)	*OECD guideline 403 did not exist at the time*
Stability of test compound in test atmosphere	*No presence or absence of aerosol reported. Probably not present*
Use of vehicle (other than air)	*Dry air*
Whole body / nose-only (incl. head/nose-only) exposure	*Probably whole-body (not explicitly specified)*
Type of restrainer	*No restrainers mentioned*
Pressure distribution.	*Chamber operated at 765-774 mmHg; pressure distribution not provided*
Homogeneity of test atmosphere in breathing zone of animals	*Test atmosphere was generated by passing a stream of clean, dry air over the undiluted material in a gas washing bottle, and introduced directly into the exposure chamber. Additional air was passed directly into the exposure chamber*
Number of air changes per hour	*Air flow was 77-201 ℓ/min through a 1.6 m^3 chamber, which equals 2.9-7.5 air changes/h*
Equilibration time (t95)	*t95 = 24-62 minutes.*
Start of exposure relative to equilibration	*No mention if complete equilibration was reached before animals were placed in the exposure chamber*
Actual concentration measurement	*No concentration measurement. Nominal concentrations reported at about 0.2% of the Saturated Vapor Concentration*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	*No aerosol formation reported*
Assessment of Reliability	***C*** *Only one exposure duration, nominal concentrations, unclear if chamber was equilibrated before start of exposure*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Nominal	Adjusted		Male	Female
Rat	500		60	0/5	0/5
	560		60	4/5	0/5
	670		60	5/5	2/5
	900		60	5/5	4/5
	1060		60	5/5	5/5

29 of 30 fatalities took place on the day of exposure and the following day.

Probit function

The probit function and associated LC-values have been calculated using the DoseResp program (Wil ten Berge, December 2006) as

$Pr = a + b \times lnC\ d \times S$

with C for concentration in mg/m^3 and S for sex (0 = female, 1 = male).

Probit function	Species	a	b	d
Sex as covariate	Rat	*-46.1*	*7.73*	*2.40*
Sexes combined	Rat	*-26.7*	*4.91*	

The LC_{50} values for both sexes did not differ by more than a factor of 2. This does not support the proposition that sex differences exist in the lethal response. For this reason the data from both sexes were pooled and analysed to derive the animal probit function.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. Male	LC_{50} (mg/m^3) 95%-C.I. Female	LC_{50} (mg/m^3) 95%-C.I. Combined
60	543 (480 - 605)	741 (649 – 864)	632 (480 – 905)

No C × t probit function could be calculated from these data alone.

Study ID: C.2

Author, year: **BASF 1980**
Substance: methyl chloroformate
Species, strain, sex: Male and female Sprague-Dawley rats
Number/sex/conc. group: 10 / sex / concentration
Age and weight: age unspecified, weight 185 ± 15 grams
Observation period: 14 days

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*OECD GLP did not exist at the time*
Study carried out according to guideline(s)	*OECD guideline 403 did not exist at the time*
Stability of test compound in test atmosphere	*No mention of aerosol formation / condensation or hydrolysis*
Use of vehicle (other than air)	*Air*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution.	*'Slightly below atmospheric pressure'.*
Homogeneity of test atmosphere in breathing zone of animals	*Test substance was continuously fed to a vaporizer head and evaporated at 45°C, mixed with fresh air and introduced into the chamber (200 liter)*
Number of air changes per hour	*Not specified*
Equilibration time (t95)	*t95 cannot be determined because of unknown airflow*
Start of exposure relative to equilibration	*No mention if complete equilibration was reached before animals were placed in the exposure chamber*
Actual concentration measurement	*Sampling location immediately adjacent to animals' noses. Analysis by gas chromatography; actual concentration was 9.8-35.1% of nominal*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	*Not applicable*
Assessment of Reliability	***C*** *Only one exposure duration. Possibly issues with generation or analysis of test atmosphere*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Nominal	Actual		Male	Female
Rat	60	6	240	0/10	0/10
	250	53	240	5/10	3/10
	490	120	240	10/10	10/10
	370	130	240	10/10	7/10

The actual-to-nominal ratio was low and highly variable (10% - 35%) compared to other studies where such information was available. This raises questions as to the quality of the generation system and/or the analysis of the test atmosphere.

Probit function

The probit function and associated LC-values have been calculated using the DoseResp program (Wil ten Berge, December 2015) as

$Pr = a + b \times lnC + d \times S$

with C for concentration in mg/m^3 and S for sex (0 = female, 1 = male).

Probit function	*Species*	*a*	*b*	*d*
Sex as covariate	*Rat*	*-4.02*	*2.10*	*0.86*
Sexes combined	*Rat*	*-2.78*	*1.90*	

The LC_{50} values for both sexes did not differ by more than a factor of 2. This does not support the proposition that sex differences exist in the lethal response. For this reason the data from both sexes were pooled and analysed to derive the animal probit function.

The derived LC_{50} values appear to be much lower than those in other studies. The authors report an LC_{50} of 60 mg/m^3 for sexes combined, identical to the value calculated for this review.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. Male	LC_{50} (mg/m^3) 95%-C.I. Female	LC_{50} (mg/m^3) 95%-C.I. Combined
240	48.6 (28.9 – 66.4)	73.1 (50.4 – 94.6)	59.7 (40.2 – 73.9)

An additional analysis using the nominal concentrations showed that the calculated probit fit these data well, and produced a 240-min LC_{50} of 241 mg/m^3 for males, 301 mg/m^3 for females and an LC_{50} of 270 mg/m^3 for sexes combined.

No C × t probit function could be calculated from these data alone.

Study ID: C.3

Author, year: **Carpenter 1982**
Substance: methyl chloroformate
Species, strain, sex: male Swiss-Webster mice
Number/sex/conc. group: 4 / concentration
Age and weight: unspecified
Observation period: unspecified, but at least 20 hours

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*No GLP statement provided*
Study carried out according to guideline(s)	*Study was designed as an RD_{50} study, and therefore not compliant with OECD guideline 403*
Stability of test compound in test atmosphere	*Probably aerosol present from the test atmosphere generation system*
Use of vehicle (other than air)	*Air*
Whole body / nose-only (incl. head/nose-only) exposure	*Head-only*
Type of restrainer	*Body plethysmopgraph*
Pressure distribution.	*No information on pressure distribution provided*
Homogeneity of test atmosphere in breathing zone of animals	*Test material was delivered at a known rate to an aerosol generator and directed into a 9 ℓ steel chamber with probably 4 mice exposed simultaneously*
Number of air changes per hour	*Flow was 20 ℓ/min minute for (most likely) 4 animals*
Equilibration time (t95)	*t95 = 1.35 minutes*
Start of exposure relative to equilibration	*Probably at start of concentration build-up, after a 10-minute fresh air control period*
Actual concentration measurement	*Nominal concentration assessment.*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	*Not reported*
Assessment of Reliability	***C*** *Only one exposure duration, unknown but probably too short observation period, insufficient info on exposure generation and characterization*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	% decrease respiratory rate	Lethality
	Measured	Adjusted			
Mouse	64.9	NA	30	13.2%	
	98.3		30	26.0%	
	138		30	33.3%	
	197		30	46.3%	1 / 4
	295		30	63.6%	1 / 4
	491		30	80.0%	4 / 4
	491		30	82.1%	3 / 4

Probit function

Due to the nature of the data no probit function and LC_{50} value have been calculated for this study. The derived RD_{50} value was reported to be 206 (186 - 229) mg/m^3. At exposures to a concentration close to 206 mg/m^3 1 of 4 test animals died within 6 hours following exposure.

A review of the breathing pattern suggested that at the 491 mg/m^3 exposure level 3 out of 4 animals showed a pulmonary irritation breathing pattern (Carpenter 1982a).

Study ID: Other C studies

Death occurred in 11/12, 5/6 and 6/6 rats exposed to an atmosphere 'essentially enriched or saturated' for 3, 10 and 30 minutes respectively (BASF 1975).

Death occurred in 12/12 rats exposed to 72400 mg/m^3 methyl chloroformate vapour at 20 °C for 3 minutes (BASF 1981).

The final AEGL TSD reports a 2-hour LC_{50} value in mice of 91 mg/m^3 by Gurova (1977). No other experimental details were provided.

Death occurred in 10/10 rats exposed to an atmosphere 'essentially enriched or saturated' 20°C for 3 minutes (Hoechst 1985).

In a publication with toxicological data on many chemicals, Vernot (1977) reported 1-hour LC_{50} values in rats for methyl chloroformate of 170 mg/m^3 for males and 199 mg/m^3 for females. Many relevant details of the study design were not provided.

At the WARF institute (1972) 10 rats/group were exposed for 1 hour at concentrations of 256000, 37500, 11390 and 2840 mg/m^3. All test animals died within 18 hours.

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