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
Allyl chloride	**107-05-1**

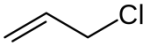
This document describes the derivation of a probit function for application in a quantitative risk analysis (QRA). The probit function has been derived according to the methodology described in RIVM report 2015-0102.

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 "interim", pending a decision on its formal implementation.

The decision on actual implementation depends on the results of a further consequence analysis.

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

Technical support document Allyl chloride



1. Substance identification

CAS-number:	107-05-1
IUPAC name:	3-chloropropene
Synonyms:	allyl chloride, chlorallylene, 1-chloro-2-propene
Molecular formula:	C_3H_5Cl
Molecular weight:	76.5 g/mol
Physical state:	liquid (at 20°C and 101.3 kPa)
Boiling point:	43-49°C (at 101.3 kPa)
Vapour pressure:	39.5 kPa (at 20°C)
Saturated vapor conc:	395,000 ppm = 1260 g/m^3 (at 20°C)
Conversion factor:	1 mg/m^3 = 0.314 ppm (at 20°C and 101.3 kPa)
	1 ppm = 3.182 mg/m^3 (at 20°C and 101.3 kPa)
Labelling:	H302-312-315-319-332-335-341-351-373

2. Mechanism of action and toxicological effects following acute exposure[1]

Acute effects: The main target organs and tissues for inhalation exposure to allyl chloride are the respiratory tract, skin and eyes. The health endpoints are irritation to the skin, eyes and respiratory tract, but also damage to the liver and kidneys and central nervous system effects may result from allyl chloride exposure. Symptoms of high exposure are drowsiness, lacrimation, salivation, weakness, apnoea, pulmonary haemorrhage, oedema and pneumonia. Lethality likely results from respiratory failure.

Long-term effects: Chronic exposure produces the same effects as seen at acute exposures. Liver and kidney toxicity have been observed in repeated dose studies in several species.

3. Human toxicity data

No informative reports on human toxicity following acute inhalation exposure were identified in which details about both 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 interim TSD, ERPG document and EU RAR and reference database for allyl chloride, 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.

[1] AEGL (interim 2008), ERPG (2006) and Chemiekaarten (2016).

Animal lethal toxicity data focused on acute exposure are described in Appendix 1. A total of 4 studies were identified -with 10 datasets for 5 species- with data on lethality following acute inhalation exposure. None of the datasets were assigned status A or B1 for deriving the human probit function, 2 datasets were assigned status B2 and 8 were assessed to be unfit (status C) for human probit function derivation.

Sensory irritation

One 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 Allyl chloride*

Species/strain	RD_{50} (mg/m^3)	Exposure duration (min)	Author/year
mice	7,414 [P]	10	Nielsen and Bakbo, 1985

P: a plateau was reached

5. Probit functions from individual studies

All available acute lethality data on Allyl chloride are displayed in Figure 1.

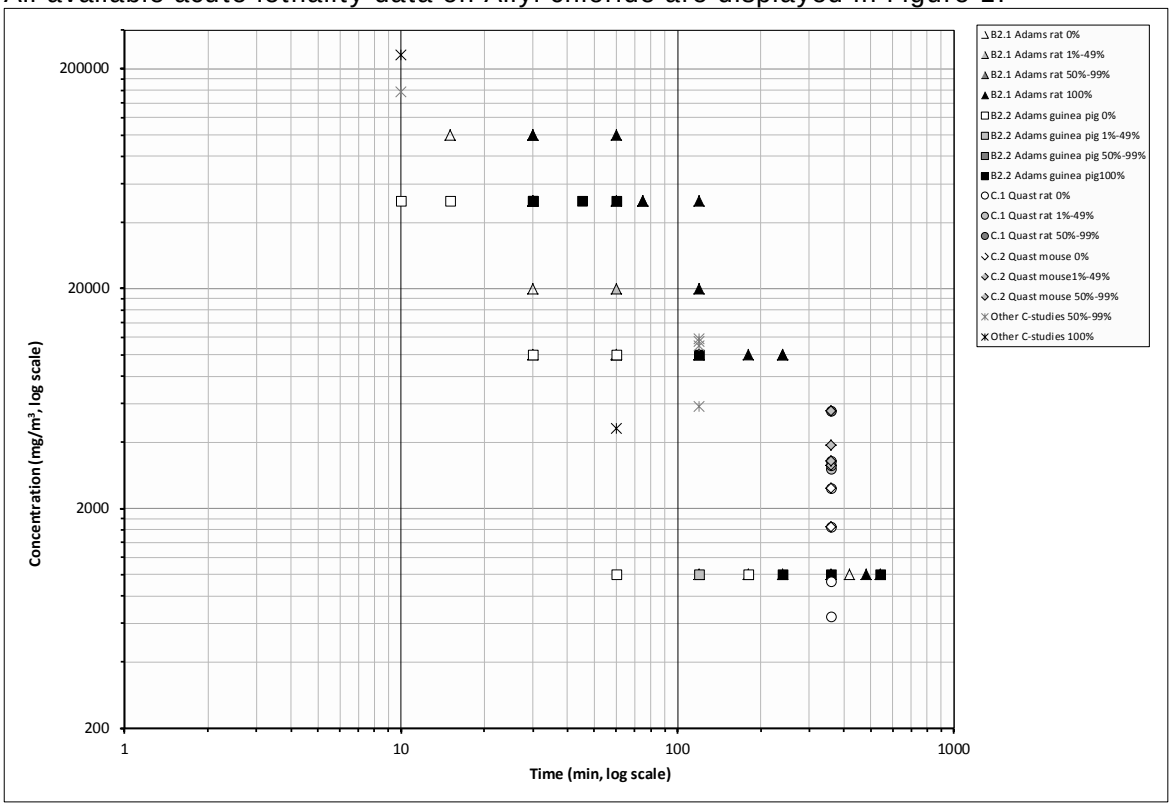


Figure 1 *All available acute lethality data for allyl chloride.*

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

It was not possible to derive a probit function for allyl chloride based on studies with A quality. Therefore, the probit function was derived using data from the studies with B2 quality listed in the table below.

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.

Table 2 *Data selected for initial analysis of the animal probit function of allyl chloride.*

Study ID	Species	Probit (C in mg/m^3, t in min)	LC_{50}, 30 minutes (mg/m^3) 95% C.I.	n-value 95% C.I.
B2.1	Rat	-37.8 + 2.52×lnC + 4.21×lnt	80720 (59390-113100)	0.600 (0.540-0.660)
B2.2	Guinea pig	-31.4 + 2.07×lnC + 4.19×lnt	45900 (31650-64370)	0.493 (0.431-0.554)

The data of the rat study B2.1 and guinea pig study B2.2 of Adams *et al*. (1940) are presented graphically below.

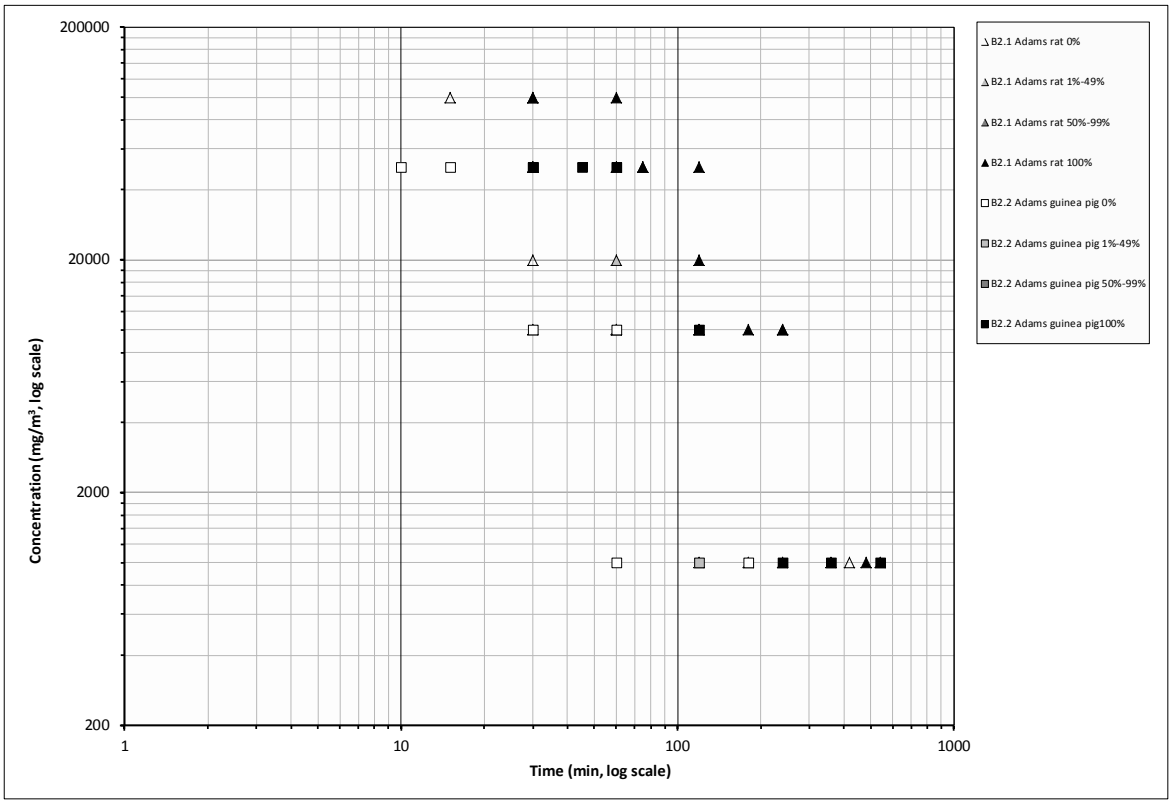


Figure 2 *Data selected for the initial analysis for the derivation of the animal probit function of allyl chloride*

Based on visual inspection of the data from the rat study B2.1 and guinea pig study B2.2 of Adams *et al*. (1940) and rather similar probit function results, the data from studies B2.1 and B2.2 were selected for the final dataset for the derivation of the animal probit function. The reason for including these studies is that the studies are considered to be of sufficient quality, including sufficient C x t combinations.

Figure 3 provides an overview of LC_{50} values and LC_{50}-time relationships for all studies in the final analysis. The data that were selected for final analysis of the animal probit function are presented in Table 3 and Figure 4.

The final data eligible for calculating the animal probit function contains two datasets from one study and includes data from two animal species.

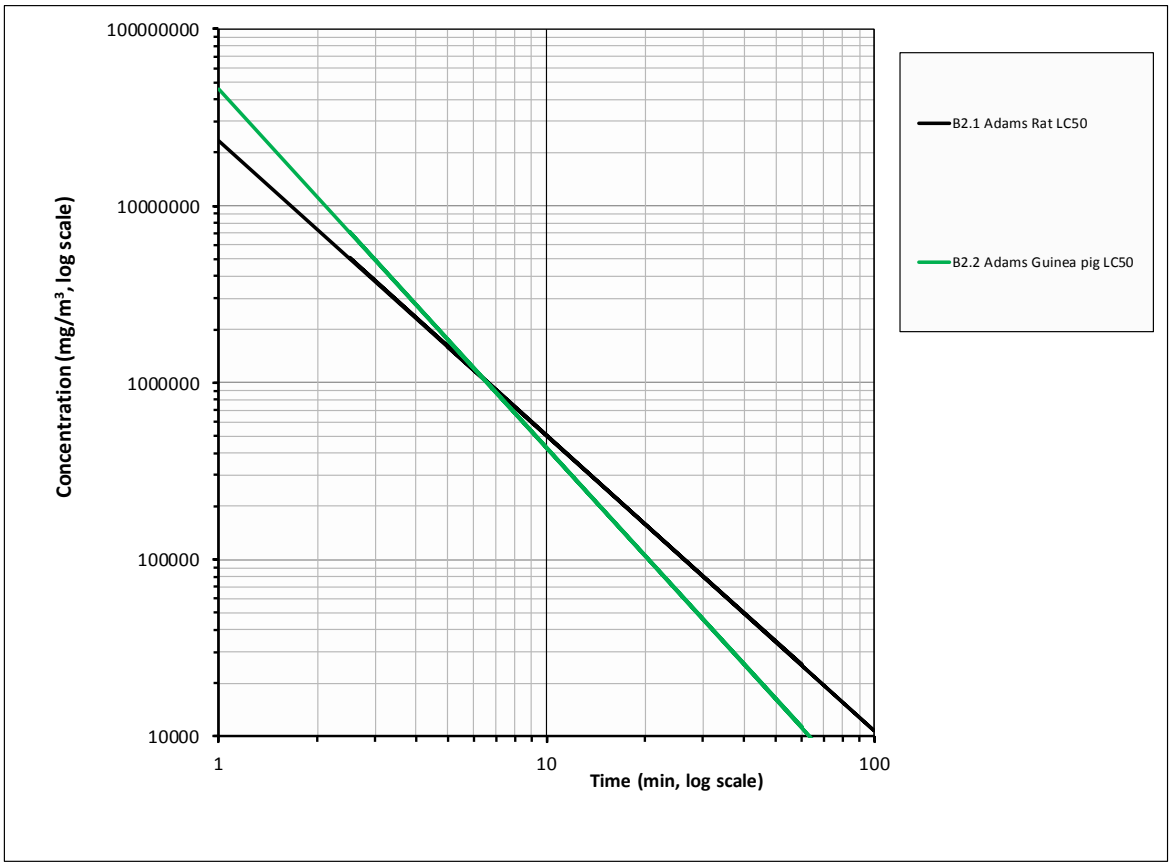


Figure 3 *LC_{50} values of B2 datasets for allyl chloride, over time where available.*

Table 3 *Data selected for the derivation of the animal probit function of allyl chloride (identical to table 2).*

Study ID	Species	Probit (C in mg/m^3, t in min)	LC_{50}, 30 minutes (mg/m^3) 95% C.I.	n-value 95% C.I.
B2.1	Rat	-37.8 + 2.52×lnC + 4.21×lnt	80720 (59390-113100)	0.600 (0.540-0.660)
B2.2	Guinea pig	-31.4 + 2.07×lnC + 4.19×lnt	45900 (31650-64370)	0.493 (0.431-0.554)

The data of the selected datasets are presented graphically below.

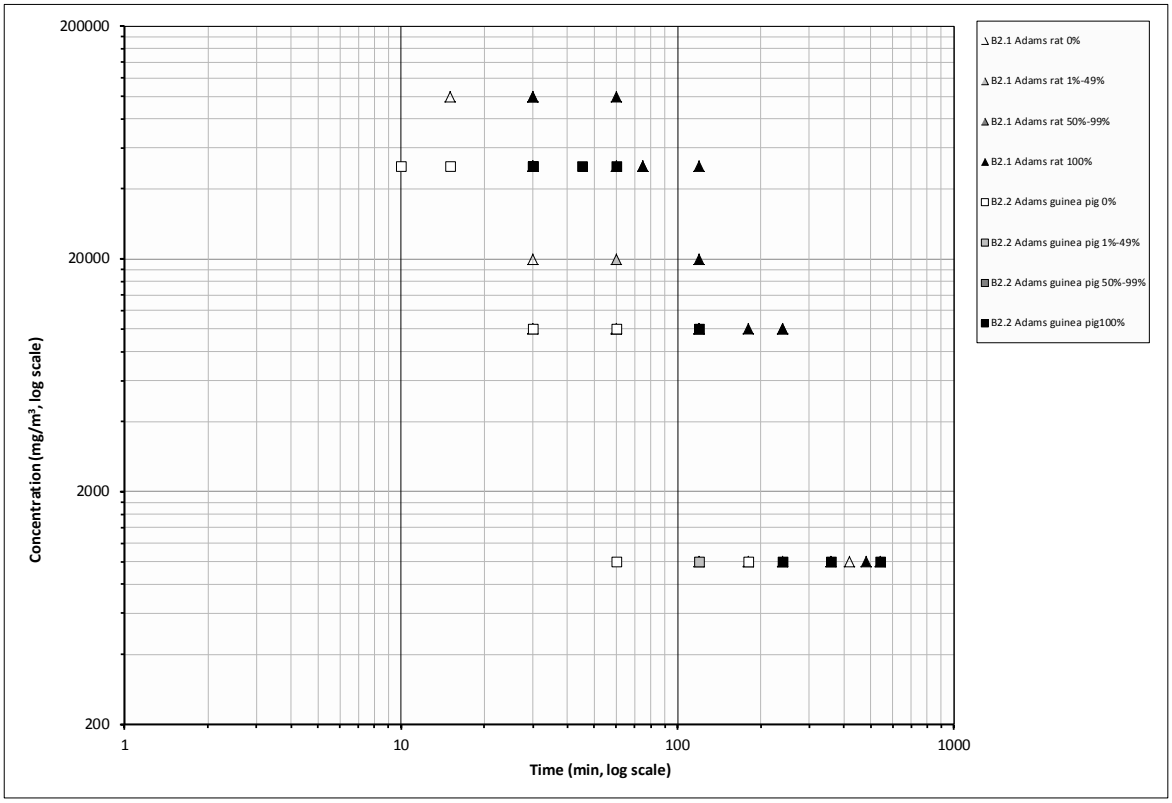


Figure 4 Final data selected for derivation of the animal probit function of allyl chloride (identical to figure 2).

6. Derivation of the human probit function

To derive the human probit function the results from rat study B2.1 and guinea pig study B2.2 (Adams et al., 1940) have been used to derive a point of departure as outlined above.

In the study of Adams et al. (rat study B2.1 and guinea pig study B2.2), different exposure designs were used; for some exposures lasting less than one hour a 10 L chamber was used, with 2 animals per exposure, for other exposures lasting 30 min or longer a 154 L chamber was used, with 5 animals per exposure; the publication does not allow to differentiate with certainty which exposure-response data were obtained by each method. Further information about the exact exposure design for the <60 min durations were lacking and thus the reliability of the <60 min data is uncertain. However, probit analyses of the datasets including all data, excluding <30 min data or excluding <60 min data showed similar results and the LC_{50} values for the various datasets (i.e. all data, excl. <30 min data, excl. <60 min data) did not differ by more than a factor of 2. Therefore, it was considered appropriate to use the results of analyses with the entire dataset of Adams et al. (studies B2.1 and B2.2) for the derivation of probit functions.

First, the arithmetic mean n-value was calculated from studies B2.1 and B2.2 (Adams et al, 1940). The species-specific n-value was 0.600 for the rat, 0.493 for the guinea pig. The arithmetic mean n-value across species is the simple arithmetic mean of the species-specific mean n-values, without weight and was calculated to be 0.547.

Finally, the species-specific geometric mean LC_{50}-values were calculated from the available LC_{50} values of studies B2.1 and B2.2. The 30-min species-specific LC_{50}-value was 80720 mg/m^3 for the rat, 45900 mg/m^3 for the guinea pig. Finally, a geometric

mean overall LC_{50}-value was calculated. The overall formula for the geometric mean of time-scaled LC_{50}-values is as follows:

$$\overline{LC_{50}} = \left[\prod_{j=1}^{s}\left(\prod_{i=1}^{m} LC_{50,i}\right)^{1/m}\right]^{(1/s)}$$

With $\overline{LC_{50}}$ = geometric mean LC_{50}-value across species
$LC_{50,i}$ = LC_{50}-value of study i.
m = number of observations on LC_{50}-values within a species (i=1…m).
s = number of species for which LC_{50}-values are pooled (j= 1…s).

The Point of Departure for the human probit function is a 30-minute geometric mean animal LC_{50} value of 60869 mg/m^3 and an arithmetic mean n-value of 0.547.

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	Default
Nominal concentration	1	Rat study B2.1 and guinea pig study B2.2 presented no actual concentrations but target concentrations. Nominal concentrations were calculated but not reported; target concentrations were <25% of the saturated vapour concentration. As such it was assumed that actual concentrations were close to nominal concentrations.
Adequacy of database:	2	Point of departure is based on two B2 studies with sufficient concentration-time combinations. However, no A or B1 studies are available. Further, there is some uncertainty on the actual exposure concentrations since no analytical measurements were performed and nominal concentrations were not reported.

The estimated human equivalent 30-minute LC_{50} value is 60869 / 6 = **10145 mg/m^3**.

The calculated n-value was **0.547** (arithmetic mean value of rat study B2.1 and guinea pig study B2.2 (Adams et al., 1940)). Assuming a regression coefficient (b×n) of 2 for the slope of the curve, the b-value can be calculated as 2 / n = **3.66**.

The human probit function is then calculated on the human equivalent 30 min LC_{50} using the above parameters to solve the following equation to obtain the a-value (the intercept): $5 = a + 3.66 \times \ln(10145^{0.547} \times 30)$ resulting in the a-value of **-25.90**.

$Pr = -25.90 + 3.66 \times \ln (C^{0.547} \times t)$ with C in mg/m^3 and t in min.

The derived human probit function has a scientifically acceptable basis. The probit function is based on one study in the rat with B2 quality and one study in the guinea pig with B2 quality, including in total 37 concentration-time combinations, exposure durations varying from 10 to 540 minutes, and response rates in the range from 0 to 100% mortality.

The calculated human 60 min $LC_{0.1}$ (Pr = 1.91) calculated with this probit equation is 605 mg/m^3 and the calculated human 60 min LC_1 (Pr = 2.67) is 885 mg/m^3.

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

Estimated level	30 min (mg/m^3)	60 min (mg/m^3)
0.1% lethality, this probit	2150	605
1% lethality, this probit	3142	885
AEGL-3[2] (2008, interim)	573	445
ERPG-3[2] (2006)	-	955
LBW (2015)	3200	1000

Compared with equivalent (inter)national guideline levels as presented in the table above, the lethal levels derived with this probit function are comparable (with the exception of 30 min AEGL-3).

[2] AEGL and ERPG values were converted from ppm to mg/m^3 with the conversion factor calculated in section 1. Therefore, the AEGL and ERPG values in mg/m^3 can deviate slightly from those reported in the AEGL and ERPG TSDs.

Appendix 1 Animal experimental research

Study ID: B2.1

Author, year: Adams et al., 1940

Substance: Allyl chloride
Species, strain, sex: rat, albino, sex not specified
Number/sex/conc. group: 4 or 5/conc. group
Age and weight: age: 60-100 days, bw not specified
Observation period: 4 weeks or until death occurred

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*GLP did not exist at the time*
Study carried out according to OECD 403 guideline(s)	*OECD guideline 403 did not exist at the time*
Stability of test compound in test atmosphere	*No information*
Use of vehicle (other than air)	*N/A*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution	*No information*
Homogeneity of test atmosphere in breathing zone of animals	*It was stated that two exposure methods were used:* *1. For most exposures, lasting 30 min or longer, a group of 5 animals was placed in a monel wire cage on 6-inch legs within a glass-monel chamber of 154 L capacity.* *2. For a few exposures lasting less than 1 hour, 2 animals at a time were exposed in a 10 L glass jar.* *For the first exposure method, the substance was sprayed onto the sides of the chamber in a preset amount to build up the vapour concentration. Allyl chloride was added to the airflow to maintain the concentration in the chamber. To do so, allyl chloride was metered by a displacement pump into a warmed monel pipe through which flowed the air entering the chamber.* *No information concerning test atmosphere generation was stated for the second exposure method.*

Number of air changes per hour	*For the first exposure method the air flow was between 15 to 30 L/min in a 154 L chamber, resulting in 5.8 to 11.7 air changes per hour.* *No information concerning number of air changes was stated for the second exposure method.*
Equilibration time (t95)	*First exposure method: 15-31 min* *Second exposure method: insufficient information to calculate t95*
Start of exposure relative to equilibration	*No information*
Actual concentration measurement	*No analytical measurements were performed.* *For the first exposure method, the concentration of vapour was determined by the output of the allyl chloride pump and by the airflow through the chamber (the resulting nominal concentrations were not presented, though it is stated by study authors that "the output of allyl chloride was checked by collection and weighing, and was quite constant)". However, it is not clear to what extent the nominal concentration differed from the target concentration.* *No information concerning (nominal) concentration determination was stated for the second exposure method.*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*N/A*

Assessment of Reliability	***B2*** *The study included many C × t combinations. However, only target concentrations were reported and therefore the study was not given the A-status.* *Allyl chloride has a high vapour pressure. For a vapour, it is expected that the nominal concentration will be close to the actual concentration unless condensation has occurred. Calculations of the ratio of the highest target concentration vs. saturated vapour concentration (SVC), which is below 0.25 (i.e. 100,000/1,260,000 = 0.079), further confirms this.* *However, it is not clear to what extent the nominal (and thus the actual) concentration differed from the target concentration.* *An A status could not be assigned since actual concentrations were not reported, consequently the study is assigned the B2-status. Moreover, two different exposure designs were used in the study and there is some uncertainty on the actual exposure concentrations.*

Additional remark: The authors presented information on the time of death as follows:
1×10^3 mg/m^3: "All deaths occurred within 24 hours"
10×10^3 mg/m^3: "With one exception all guinea pigs deaths occurred after exposure. Rats behaved similarly except that more died during exposure."
20×10^3 mg/m^3: All deaths occurred within 24 hours."
50×10^3 mg/m^3: "Deaths usually occurred within a few hours, all within 24 hours."
100×10^3 mg/m^3: "All died in a short time."

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality
	Measured	Adjusted		
				Dead/tested
Rat	1×10^3		120	0/5
	1×10^3		180	0/5
	1×10^3		240	1/5
	1×10^3		360	1/5
	1×10^3		420	0/5
	1×10^3		480	5/5
	1×10^3		540	5/5
	10×10^3		30	0/5
	10×10^3		60	0/5
	10×10^3		60	0/5
	10×10^3		120	4/5
	10×10^3		120	2/5
	10×10^3		180	5/5

	10 x 10^3		240	5/5
	10 x 10^3		240	5/5
	20 x 10^3		30	0/5
	20 x 10^3		60	1/5
	20 x 10^3		120	5/5
	50 x 10^3		30	0/4
	50 x 10^3		30	0/5
	50 x 10^3		60	4/5
	50 x 10^3		75	5/5
	50 x 10^3		75	4/4
	50 x 10^3		120	5/5
	100 x 10^3		15	0/4
	100 x 10^3		30	4/4
	100 x 10^3		30	5/5
	100 x 10^3		60	5/5

Probit function

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

$Pr = a + b \times \ln C + c \times \ln t$

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

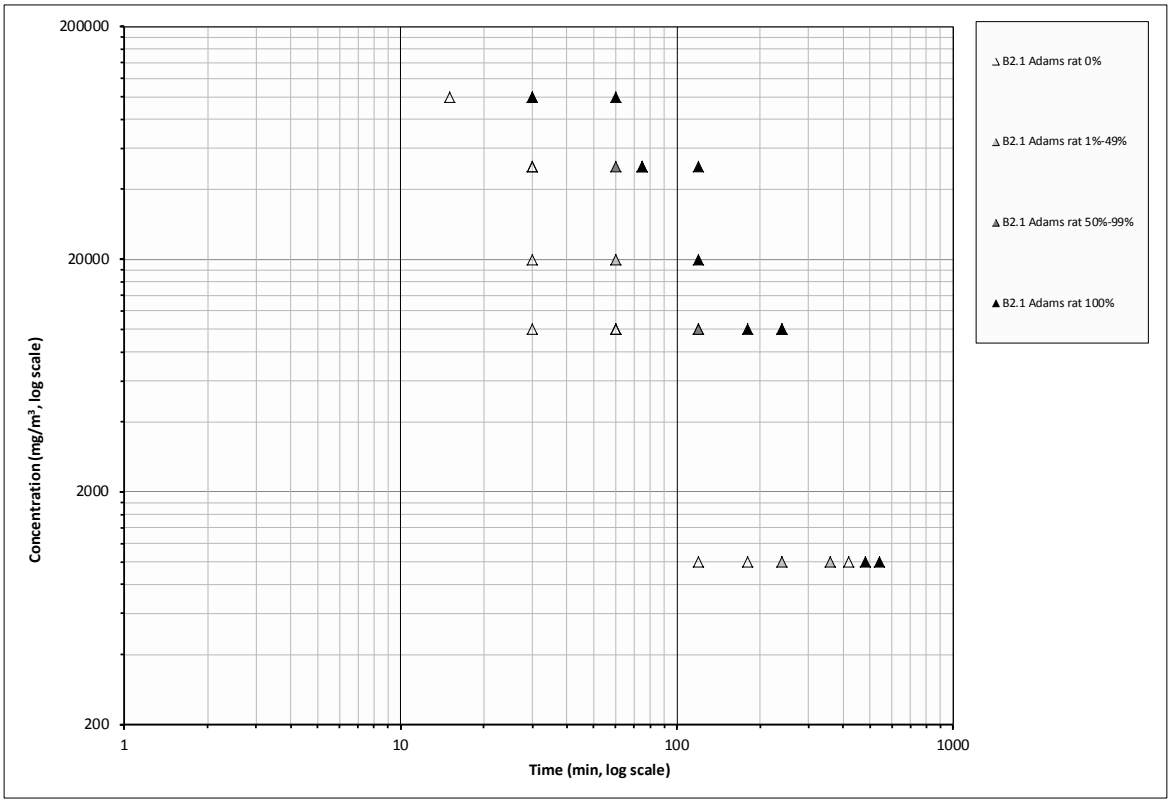
Probit function	Species	a	b	c	n-value
Data of all exposure durations included	Rat	-37.8	2.52	4.21	0.600 (0.540 – 0.660)
Excl. <30 min data	Rat	-37.5	2.51	4.17	0.601 (0.540 – 0.662)
Excl. <60 min data	Rat	-34.1	2.22	3.95	0.562 (0.494 – 0.631)

Different exposure designs were used; for some exposures lasting less than one hour a 10 L chamber was used, with 2 animals per exposure, for other exposures lasting 30 min or longer a 154 L chamber was used, with 5 animals per exposure; the publication does not allow to differentiate with certainty which exposure-response data were obtained by each method. Further information about the exact exposure design for the <60 min durations were lacking and thus the reliability of the <60 min data is uncertain. However, probit analyses of the datasets including all data, excluding <30 min data or excluding <60 min data showed similar results and the LC_{50} values for the various datasets (i.e. all data, excl. <30 min data, excl. <60 min data) did not differ by more than a factor of 2. Therefore, it was considered appropriate to use the results of analyses with the entire dataset for the derivation of probit functions.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. All data	LC_{50} (mg/m^3) 95%-C.I. Excl. <30 min data	LC_{50} (mg/m^3) 95%-C.I. Excl. <60 min data
10	503300 (317300-862900)	499800 (307400-863300)	718400 (350000-1434000)
30	80720 (59390-113100)	80350 (58100-113100)	101900 (62810-159200)

60	25440 (20090-32230)	25360 (19780-32240)	29710 (20970-40300)

A graphical overview of the data is presented below. Each concentration-time combination (with 4 or 5 animals) represents one point in the plot.



Study ID: B2.2

Author, year: Adams et al., 1940
Substance: Allyl chloride
Species, strain, sex: guinea pig, strain and sex not specified
Number/sex/conc. group: 4 or 5/conc. group
Age and weight: age not specified, bw: 300 to 400 g
Observation period: 4 weeks or until death occurred

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*GLP did not exist at the time*
Study carried out according to OECD 403 guideline(s)	*OECD guideline 403 did not exist at the time*
Stability of test compound in test atmosphere	*No information*
Use of vehicle (other than air)	*N/A*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution	*No information*
Homogeneity of test atmosphere in breathing zone of animals	*It was stated that two exposure methods were used:* *3. For most exposures, lasting 30 min or longer, a group of 5 animals was placed in a monel wire cage on 6-inch legs within a glass-monel chamber of 154 L capacity.* *4. For a few exposures lasting less than 1 hour, 2 animals at a time were exposed in a 10 L glass jar.* *For the first exposure method, the substance was sprayed onto the sides of the chamber in a preset amount to build up the vapour concentration. Allyl chloride was added to the airflow to maintain the concentration in the chamber. To do so, allyl chloride was metered by a displacement pump into a warmed monel pipe through which flowed the air entering the chamber.* *No information concerning test atmosphere generation was stated for the second exposure method.*
Number of air changes per hour	*For the first exposure method the air flow was between 15 to 30 L/min in a 154 L chamber, resulting in 5.8 to 11.7 air changes per hour.* *No information concerning number of air changes was stated for the second exposure method.*

Equilibration time (t95)	*First exposure method: 15-31 min* *Second exposure method: insufficient information to calculate t95*
Start of exposure relative to equilibration	*No information*
Actual concentration measurement	*No analytical measurements were performed.* *For the first exposure method, the concentration of vapour was determined by the output of the allyl chloride pump and by the airflow through the chamber (the resulting nominal concentrations were not presented, though it is stated by study authors that "the output of allyl chloride was checked by collection and weighing, and was quite constant)". However, it is not clear to what extent the nominal concentration differed from the target concentration.* *No information concerning (nominal) concentration determination was stated for the second exposure method.*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*N/A*

Assessment of Reliability	***B2*** *The study included many C × t combinations. However, only target concentrations were reported and therefore the study was not given the A-status.* *Allyl chloride has a high vapour pressure. For a vapour, it is expected that the nominal concentration will be close to the actual concentration unless condensation has occurred. Calculations of the ratio of the highest target concentration vs. saturated vapour concentration (SVC), which is below 0.25 (i.e. 100000/1260000 = 0.079), further confirms this.* *However, it is not clear to what extent the nominal (and thus the actual) concentration differed from the target concentration.* *An A status could not be assigned since actual concentrations were not reported, consequently the study is assigned the B2-status. Moreover, two different exposure designs were used in the study and there is some uncertainty on the actual exposure concentrations.*

Additional remark: The authors presented information on the time of death as follows:
1 x 10^3 mg/m^3: "All deaths occurred within 24 hours"
10 x 10^3 mg/m^3: "With one exception all guine pigs deaths occurred after exposure. Rats behaved similarly except that more died during exposure."
20 x 10^3 mg/m^3: All deaths occurred within 24 hours."
50 x 10^3 mg/m^3: "Deaths usually occurred within a few hours, all within 24 hours."
100 x 10^3 mg/m^3: "All died in a short time."

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality
	Measured	Adjusted		
				Dead/tested
Guinea pig	1x10^3		60	0/5
	1x10^3		120	1/5
	1x10^3		180	0/5
	1x10^3		240	5/5
	1x10^3		360	5/5
	1x10^3		540	5/5
	10x10^3		30	0/5
	10x10^3		60	0/5
	10x10^3		120	5/5
	50x10^3		10	0/4
	50x10^3		15	0/4
	50x10^3		30	2/4
	50x10^3		30	5/5

	$50x10^3$		30	2/5
	$50x10^3$		45	4/4
	$50x10^3$		60	5/5

Probit function

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

$Pr = a + b \times lnC + c \times lnt$

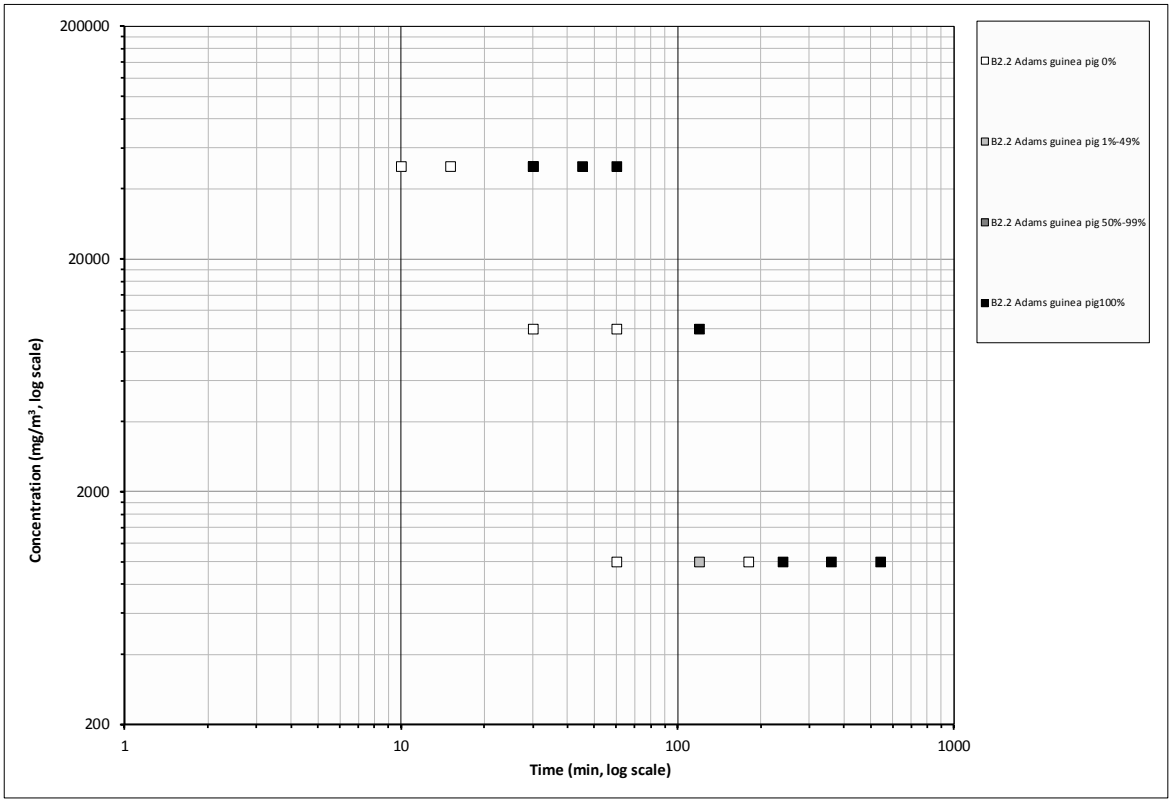
with C for concentration in mg/m^3 and t for time in minutes (0 = female, 1 = male).

Probit function	Species	a	b	c	n-value
Data of all exposure durations included	Guinea pig	-31.4	2.07	4.19	0.493 (0.431 – 0.554)
Excl. <30 min data	Guinea pig	-31.1	2.05	4.16	0.493 (0.396-0.590)
Excl. <60 min data	Guinea pig	-31.8	1.80	4.65	0.387 (0.188-0.586)

Different exposure designs were used; for some exposures lasting less than one hour a 10 L chamber was used, with 2 animals per exposure, for other exposures lasting 30 min or longer a 154 L chamber was used, with 5 animals per exposure; the publication does not allow to differentiate with certainty which exposure-response data were obtained by each method. Further information about the exact exposure design for the <60 min durations were lacking and thus the reliability of the <60 min data is uncertain. However, probit analyses of the datasets including all data, excluding <30 min data or excluding <60 min data showed similar results and the LC_{50} values for the various datasets (i.e. all data, excl. <30 min data, excl. <60 min data) did not differ by more than a factor of 2. Therefore, it was considered appropriate to use the results of analyses with the entire dataset for the derivation of probit functions.

Duration (min.)	LC_{50} (mg/m^3) 95%-C.I. All data	LC_{50} (mg/m^3) 95%-C.I. Excl. <30 min data	LC_{50} (mg/m^3) 95%-C.I. Excl. <60 min data
10	427000 (227500-807900)	424700 (42860-2894000)	1983000 (C.I. could not be determined)
30	45900 (31650-64370)	45760 (9836-112800)	116400 (C.I. could not be determined)
60	11240 (8324-14290)	11220 (2842-19900)	19460 (C.I. could not be determined)

A graphical overview of the data is presented below. Each concentration-time combination (with 4 or 5 animals) represents one point in the plot.


200000
20000
2000
200
Concentration (mg/m³, log scale)
1
10
100
1000
Time (min, log scale)
B2.2 Adams guinea pig 0%
B2.2 Adams guinea pig 1%-49%
B2.2 Adams guinea pig 50%-99%
B2.2 Adams guinea pig100%

1

Study ID: C.1

Author, year: Quast et al., 1982
Substance: Allyl chloride
Species, strain, sex: rat, CDF Fischer 344, male+female
Number/sex/conc. group: 10/sex/conc. group
Age and weight: 9-14 weeks, 131-285 grams
Observation period: 24 or 48h for the first 5 animals/conc. group, 24-168h for remaining animals

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*No GLP statement provided*
Study carried out according to OECD 403 guideline(s)	*No statement of compliance with OECD guideline 403 provided*
Stability of test compound in test atmosphere	*No information*
Use of vehicle (other than air)	*N/A*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution	*No information*
Homogeneity of test atmosphere in breathing zone of animals	*The vapour was generated by metering an amount of allyl chloride liquid into a heated vaporization flask with a precision syringe pump. The vapour was introduced with filtered air into the main chamber airflow at a rate of appr. 30 l/min.*
Number of air changes per hour	*Airflow of approximately 30 l/min in a 160 l chamber results in approximately. 11 air changes per hour.*
Equilibration time (t95)	*16 minutes*
Start of exposure relative to equilibration	*No information*
Actual concentration measurement	- *a gas chromatograph equipped with 1 ml gas sampling loops and flame ionization detector. This method was only used for the initial 644, 930 and 3,036 mg/m^3 exposures.* - *Infrared spectrophotometer was used for the remaining exposures. Constant monitoring took place.*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*N/A*
Assessment of Reliability	***C*** *Study limited to one exposure duration. Some groups had very short observation periods (24 hour). This period is considered not sufficient to cover for possible delayed deaths. Therefore, the true mortality incidence could not be ascertained.*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Measured	Adjusted		Male	Female
				Dead/tested	
Rat	644	N/A	360	0/10	0/10
	930	N/A	360	0/10	0/10
	1647	N/A	360	0/10	0/10
	2479	N/A	360	0/10	0/10
	3036	N/A	360	1/10	1/10
	3132*[#]	N/A	360	0/10	1/10
	3283[#]	N/A	360	0/10	0/10
	5553	N/A	360	1/10	10/10

* this exposure was conducted with allyl chloride from Shell Chemical Company. All other tests were conducted with material from the Dow Chemical Company.

[#] these exposures were conducted for comparison purposes using a sample of allyl chloride obtained from The Dow Chemical Company and a sample obtained from Shell Chemical Company; all animals remaining alive were necropsied at 24h post-exposure

[$] the lethality data showed that most deaths occurred during the 24h post-exposure period, though some incidental deaths were observed between 24 and 72 hour post-exposure

Probit function

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

$Pr = a + b \times \ln C + d \times S$

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

Probit function	Species	a	b	d	n-value
Sex as covariate	Rat	-28.2	3.78	1.54	-
Sexes combined	Rat	-21.7	3.12	-	-

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
360	6516 (3731 – 26,730,000)	4332 (3150 – 1,956,000)	5356 (4686 - 6822)

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.

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

Study ID: C.2

Author, year: Quast et al., 1982
Substance: Allyl chloride
Species, strain, sex: mouse, B6C3E1, male+female
Number/sex/conc. group: 10/sex/conc. group
Age and weight: 8-14 weeks, 21-28 grams
Observation period: 24 or 48h for the first 5 animals/conc. group, 24-168h for remaining animals

Evaluation of study quality

Criteria	***Comment***
Study carried out according to GLP	*No GLP statement provided*
Study carried out according to OECD 403 guideline(s)	*No statement of compliance with OECD guideline 403 provided*
Stability of test compound in test atmosphere	*No information*
Use of vehicle (other than air)	*N/A*
Whole body / nose-only (incl. head/nose-only) exposure	*Whole body*
Type of restrainer	*N/A*
Pressure distribution	*No information*
Homogeneity of test atmosphere in breathing zone of animals	*The vapour was generated by metering an amount of allyl chloride liquid into a heated vaporization flask with a precision syringe pump. The vapour was introduced with filtered air into the main chamber airflow at a rate of appr. 30 l/min.*
Number of air changes per hour	*Air flow of approximately 30 l/min in a 160 l chamber results in approximately 11 air changes per hour.*
Equilibration time (t95)	*16 minutes*
Start of exposure relative to equilibration	*No information*
Actual concentration measurement	- *a gas chromatograph equipped with 1 ml gas sampling loops and flame ionization detector. This method was only used for the initial 644, 930 and 3,036 mg/m^3 exposures.* - *Infrared spectrophotometer was used for the remaining exposures. Constant monitoring took place.*
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	*N/A*
Assessment of Reliability	***C*** *Study limited to one exposure duration. Some groups had very short observation periods (24 hour). This period is considered not sufficient to cover for possible delayed deaths. Therefore, the true mortality incidence could not be ascertained.*

Results

Species	Concentration (mg/m^3)		Exposure duration (min)	Lethality	
	Measured	Adjusted		Male	Female
				Dead/tested	
Mouse	1647	N/A	360	0/10	0/10
	2479	N/A	360	0/10	0/10
	3132*[#]	N/A	360	10/10	4/10
	3283[#]	N/A	360	8/10	2/10
	3891	N/A	360	3/10	2/10
	5553	N/A	360	10/10	10/10

* this exposure was conducted with allyl chloride from Shell Chemical Company. All other tests were conducted with material from the Dow Chemical Company.

[#] these exposures were conducted for comparison purposes using a sample of allyl chloride obtained from The Dow Chemical Company and a sample obtained from Shell Chemical Company; all animals remaining alive were necropsied at 24h post-exposure

[$] the lethality data showed that most deaths occurred during the 24h post-exposure period, though some incidental deaths were observed between 24 and 72 hour post-exposure

Probit function

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

$Pr = a + b \times \ln C + d \times S$

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

Probit function	Species	a	b	d	n-value
Sex as covariate	Rat	-24.7	3.69	-0.88	-
Sexes combined	Rat	-23.2	3.45	-	-

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
360	3131 (1949 – 4670)	3977 (2881 – 8018)	3517 (2686 - 5464)

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.

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

Study ID: other C studies

Boqin *et al*., 1982 tested the acute toxicity of allyl chloride (pure over 99% or commercial grade with 90% allyl chloride) via the oral, dermal and inhalation route. Mice (10/concentration group), rats (6/concentration group), guinea pigs (4/concentration group), rabbits (2/concentration group) and cats (2/concentration group) were exposed for two hours in a static chamber at unknown concentrations. Number of experimental groups per species were also unknown. Concentrations were analysed by gas chromatography (three times). The reported 2h-LC_{50} values (C.I.) for female mice, male rats, female rats and male guinea pigs were 11,500 (10,900-12,100), 11,000 (9,400-12,600), 11,800 (11,100-12,500), 5,800 (4,700-6,800) mg/m^3, respectively. The 2-hr lethal concentration for male rabbits and cats were 22,500 and 10,500 mg/m^3, respectively. In general, deaths that occurred, were observed within 24 hours after exposure. The signs of intoxication were in general substantially similar among various species, but they were most severe in guinea pigs.

In a toxicity data sheet by Shell Chemical Corporation (1958) acute inhalation exposures in mice are described. A 10-minute exposure to 232,286 mg/m^3 allyl chloride and greater produced 12/12 deaths within 24 hours. Exposure to 156,764 mg/m^3 for 10 minutes resulted in the death of 9/12 mice 8 to 47 hours after exposure. Exposure to 4,630 mg/m^3 for one hour resulted in 4/4 deaths.

Appendix 2 Reference list

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