



Probit function technical support document

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substance name	CAS number
<b>Decalin</b>	<b>91-17-8</b>

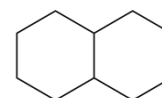
This document describes the derivation of a probit function for application in a quantitative risk analysis (QRA). The probit function has been derived according to the methodology described in RIVM report 2015-0102.

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/en/Topics/P/Probit\\_functions](http://www.rivm.nl/en/Topics/P/Probit_functions)

# 1 Technical support document Decalin



2

## 3 1. Substance identification

4	CAS-number:	91-17-8 (cis/trans isomer mixture)
5	IUPAC name:	decahydronaphthalene
6	Synonyms:	decahydronaphthalate, bicyclo(4.4.0)decane
7	Molecular formula:	C <sub>10</sub> H <sub>18</sub>
8	Molecular weight:	138.2 g/mol
9	Physical state:	liquid (at 20°C and 101.3 kPa)
10	Boiling point:	190°C (at 101.3 kPa)
11	Vapour pressure:	0.11 kPa (at 20°C)
12	Saturated vapor conc:	1100 ppm = 6324 mg/m <sup>3</sup> (at 20°C)
13	Conversion factor:	1 mg/m <sup>3</sup> = 0.174 ppm (at 20°C and 101.3 kPa)
14		1 ppm = 5.749 mg/m <sup>3</sup> (at 20°C and 101.3 kPa)
15	Labelling:	No harmonized human H-sentences

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17

## 18 2. Mechanism of action and toxicological effects following acute exposure<sup>1</sup>

20 **Acute effects:** Decalin is an irritant to the eyes, skin, and mucous membranes. CNS effects such as tremors, spasms, prostration and CNS depression might occur upon inhalation exposure.

23 **Long-term effects:** No information is available on long-term toxicity following acute exposure.

25

26

## 27 3. Human toxicity data

28 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.

31 The lowest concentration to have an effect in humans exposed by inhalation was reported to be 100 ppm (575 mg/m<sup>3</sup>), however no details are available on the type or extent of the effects (Sandmeyer 1981; BUA 1998).

34

35

## 36 4. Animal acute toxicity data

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

- 39 1. No AEGL TSD, ERPG document and EU RAR was available for decalin.
- 40 2. A full literature search covering publications from 1900 onwards was performed in 41 HSDB, MEDline/PubMed, Toxcenter, IUCLID, ECHA, RTECS, IRIS and ToxNet with 42 the following search terms:
  - 43 • Substance name and synonyms
  - 44 • CAS number
  - 45 • lethal\*
  - 46 • mortal\*
  - 47 • fatal\*
  - 48 • LC<sub>50</sub>, LC
  - 49 • probit
- 50 3. Unpublished data were sought through networks of toxicological scientists.

51

<sup>1</sup> NTP 2005; HSDB/TOXNET

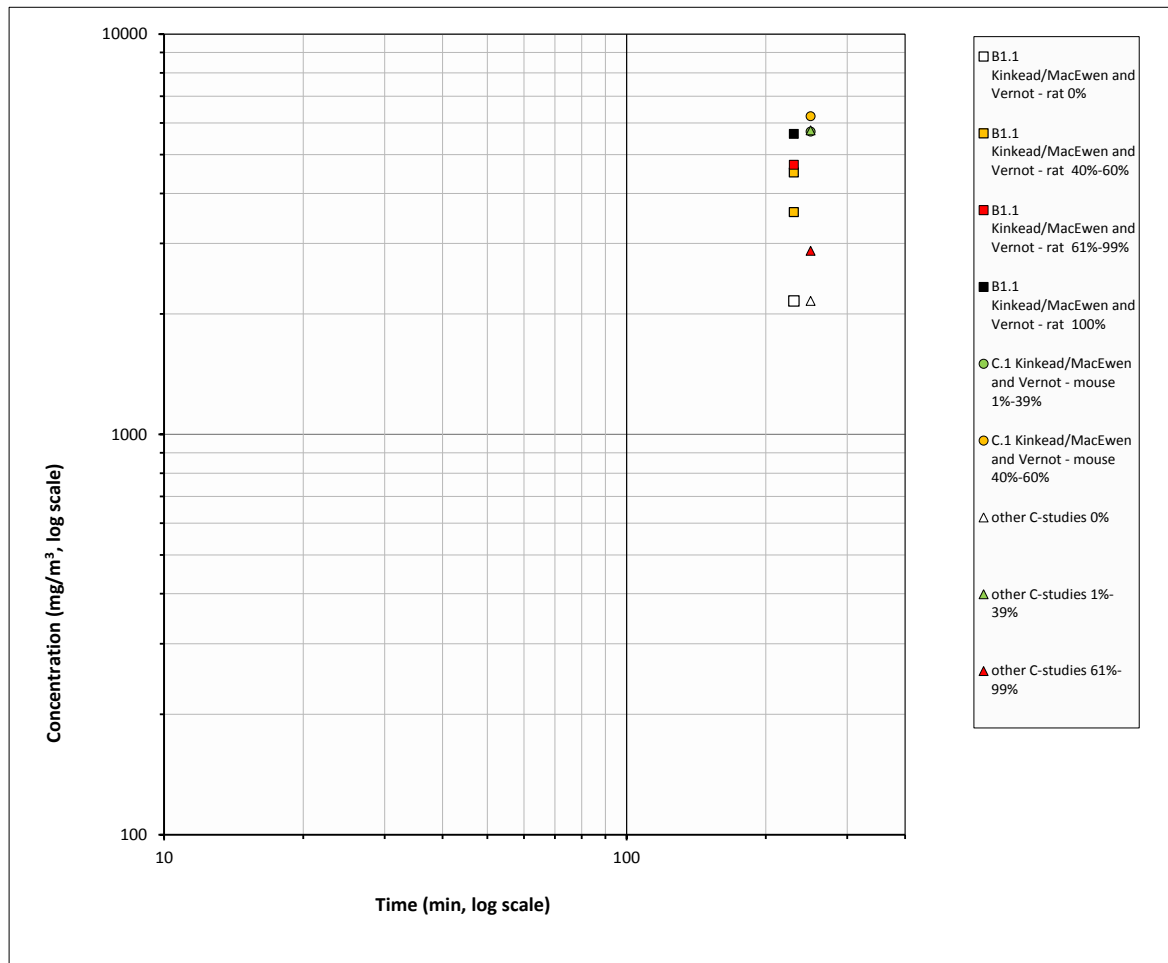
1 Animal lethal toxicity data focused on acute exposure are described in Appendix 1. A  
 2 total of 3 studies were identified -with 5 datasets for 3 species- with data on lethality  
 3 following acute inhalation exposure. None of the datasets were assigned status A, one  
 4 of the datasets was assigned status B for deriving the human probit function, and four  
 5 datasets were assessed to be unfit (status C) for human probit function derivation.

6  
 7 **Sensory irritation**

8 No studies were identified in which sensory irritation was studied.

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 10  
 11 **5. Probit functions from individual studies**

12 All available acute lethality data on decalin are displayed in Figure 1.  
 13



14 **Figure 1** All available acute lethality data for decalin

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 17 The data that were selected for initial analysis of the animal probit function are  
 18 presented in Table 1 and Figure 2.

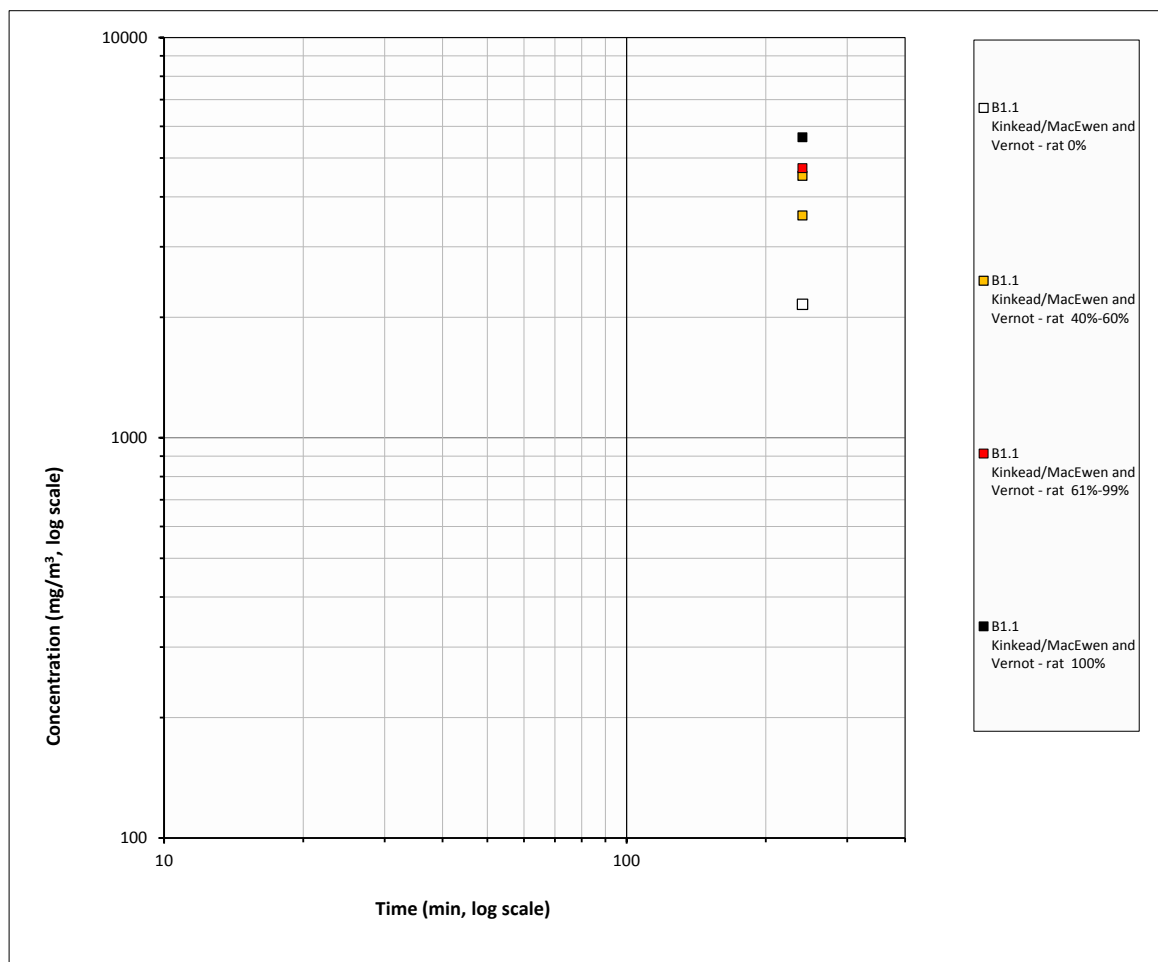
19  
 20 It was possible to derive a probit function for decalin based on the only available  
 21 study with B1 quality. However, this B1 study did not enable to produce a  
 22 concentration-time-lethality relationship.

23  
 24 Probit functions have been calculated and reported in Appendix 1 for this B1 study.  
 25 The results of the calculations are presented in Table 1.  
 26

1 **Table 1** Data selected for initial analysis of the animal probit function of decalin.

Study ID	Species	Probit (C in mg/m <sup>3</sup> , t in min)	LC <sub>50</sub> at tested exposure duration (mg/m <sup>3</sup> ) 95% C.I.	n-value 95% C.I.
B1.1	Rat	240-min LC <sub>50</sub>	4085 (2490-4770)	N/A

2  
3 The data of study B1.1 with rats are presented graphically below.  
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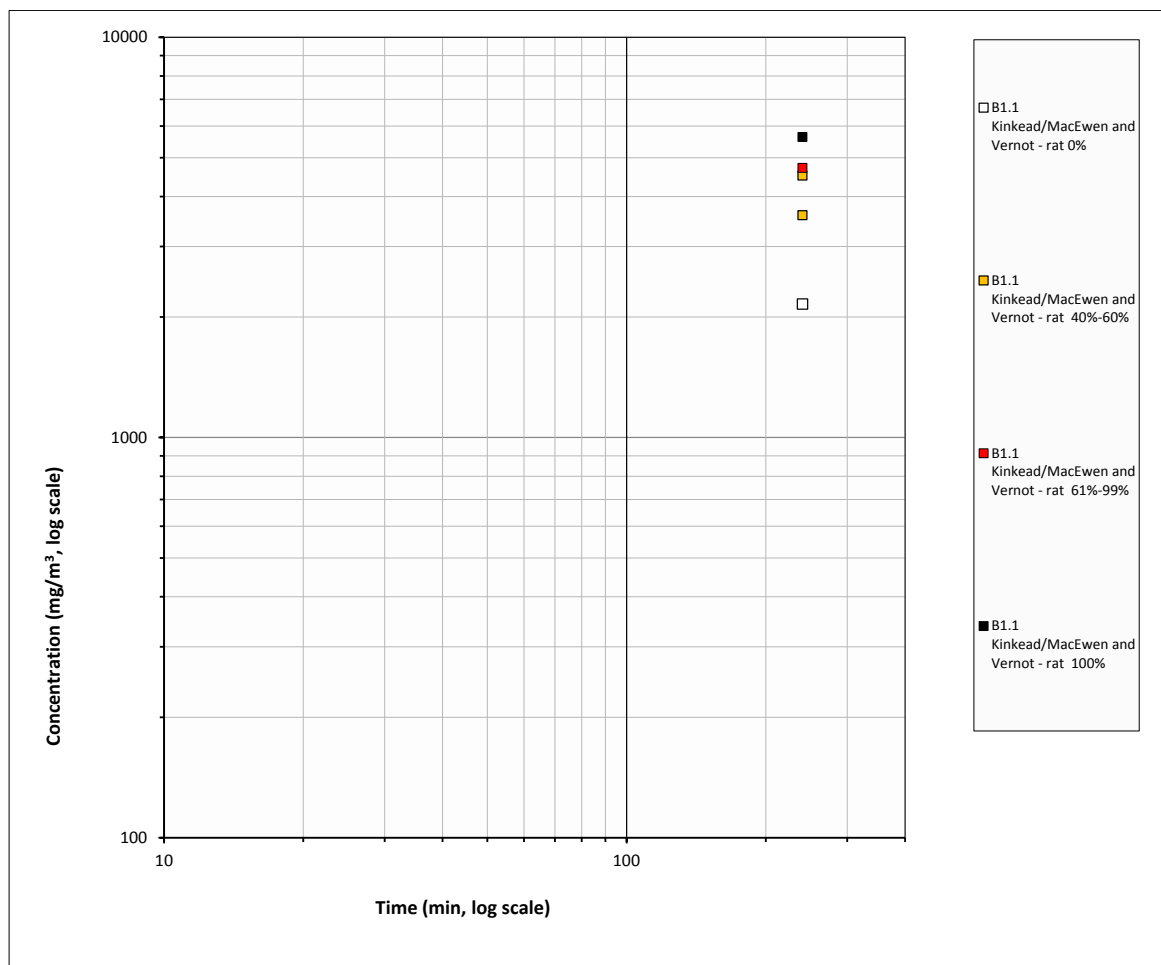
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6 **Figure 2** Data selected for the initial analysis for the derivation of the animal probit  
7 function of decalin.  
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9 Based on criteria outlined in the guideline the data from rat study B1.1 (Kinkead *et*  
10 *al.*, 1992/MacEwen and Vernot 1977) were selected for the final dataset for the  
11 derivation of the animal probit function and are presented in Table 2 and Figure 3.  
12

13 The final data eligible for calculating the animal probit function contains one dataset  
14 from one study and includes data from one animal species.  
15

16 **Table 2** Data selected for the derivation of the animal probit function of decalin  
17 (identical to table 1).

Study ID	Species	Probit (C in mg/m <sup>3</sup> , t in min)	LC <sub>50</sub> at tested exposure duration (mg/m <sup>3</sup> ) 95% C.I.	n-value 95% C.I.
B1.1	Rat	240-min LC <sub>50</sub>	4085 (2490-4770)	N/A



1  
2 **Figure 3** Final data selected for derivation of the animal probit function of Decalin  
3 (identical to figure 2).  
4  
5

6 **6. Derivation of the human probit function**

7 To derive the human probit function the results from study B1.1 (Kinkead *et al.*,  
8 1992/MacEwen and Vernot, 1977) have been used to derive a point of departure as  
9 outlined above.

10 The Point of Departure for the human probit function is a 240-minute animal LC<sub>50</sub>  
11 value of 4085 mg/m<sup>3</sup> and a default n-value of 2.

12 The human equivalent LC<sub>50</sub> was calculated by applying the following assessment  
13 factors:  
14

15 **Table 3** Rationale for the applied assessment factors.  
16  
17

Assessment factor for:	Factor	Rationale
Animal to human extrapolation:	3	default
Nominal concentration	1	B1-study with analytically determined concentrations

Adequacy of database:	2	Only one B1-dataset was found. The study was performed using only one exposure duration well outside the exposure duration target range of 30-60 min. This creates a relative large uncertainty because of extrapolation over a large range of exposure duration.
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2 The estimated human equivalent 240-minute LC<sub>50</sub> value is  $4085 / 6 = \mathbf{681 \text{ mg/m}^3}$ .

3

4 No reliable experimentally determined n-value was available, so the default n-value of  
5 **2** was used. Assuming a regression coefficient (b×n) of 2 for the slope of the curve,  
6 the b-value can be calculated as  $2 / n = \mathbf{1}$ .

7

8 The human probit function is then calculated on the human equivalent 240 min LC<sub>50</sub>  
9 using the above parameters to solve the following equation to obtain the a-value (the  
10 intercept):  $5 = a + 1 \times \ln(681^2 \times 240)$  resulting in the a-value of **-13.5**.

11

12 **Pr = -13.5 + 1 × ln(C<sup>2</sup> × t) with C in mg/m<sup>3</sup> and t in min.**

13

14 The derived human probit function has a scientifically acceptable basis. The probit  
15 function is based on one study in the rat with B1 quality, including 25 animals, an  
16 exposure duration of 240 min and response rates between 0 and 100%.

17

18 The calculated human 60-min LC<sub>0.1</sub> (Pr = 1.91) calculated with this probit equation is  
19 287 mg/m<sup>3</sup> and the calculated human 60-min LC<sub>1</sub> (Pr = 2.67) is 419 mg/m<sup>3</sup>.

20

21 **Table 3** LC-values calculated with the derived probit function compared with  
22 existing acute inhalation exposure guidelines.

Estimated level	30 min (mg/m <sup>3</sup> )	60 min (mg/m <sup>3</sup> )
0.1% lethality, this probit	405	287
1% lethality, this probit	593	419
AEGL-3	-	-
ERPG-3	-	-
LBW	-	-

23

24 A comparison with equivalent (inter)national guideline levels cannot be made.

25

## Appendix 1 Animal experimental research

### Study ID: B1.1

**Author, year:** *MacEwen and Vernot (1977); Kinkead et al. (1992)*

Substance: Decalin

Species, strain, sex: Rat, Sprague-Dawley, male

Number/sex/conc. group: 5

Age and weight: no information

Observation period: 14 days

#### Evaluation of study quality\*

Criteria	Comment
Study carried out according to GLP	<i>GLP did not exist at the time</i>
Study carried out according to OECD 403 guideline(s)	<i>OECD guideline 403 did not exist at the time</i>
Stability of test compound in test atmosphere	<i>No information</i>
Use of vehicle (other than air)	<i>N/A</i>
Whole body / nose-only (incl. head/nose-only) exposure	<i>Whole body</i>
Type of restrainer	<i>N/A</i>
Pressure distribution	<i>No information</i>
Homogeneity of test atmosphere in breathing zone of animals	<i>No information</i>
Number of air changes per hour	<i>Number of air changes not specified; 9 liter inhalation chamber</i>
Equilibration time (t95)	<i>Insufficient information to calculate t95</i>
Start of exposure relative to equilibration	<i>No information</i>
Actual concentration measurement	<i>Chamber concentrations were analysed using a hydrocarbon analyser</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	<i>N/A</i>
Assessment of Reliability	<b>B1</b> <i>Study seems to meet the standards, though limited to one exposure duration.</i>

\* Limited information concerning the study characteristics of this acute inhalation study is available. This acute inhalation study was used for concentration-ranging purposes for a 30-day repeated inhalation study and was presented together with the results of this 30-day repeated inhalation study in a different report. No specific details on study characteristics were presented in this report (MacEwen and Vernot 1978).

#### Results

Species	Concentration (mg/m <sup>3</sup> )		Exposure duration (min)	Lethality
	Measured	Adjusted		
				Male Dead/tested
Rat	2156	N/A	240	0/5
Rat	3593	N/A	240	2/5
Rat	4513	N/A	240	2/5
Rat	4714	N/A	240	4/5
Rat	5634	N/A	240	5/5

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Prior to exposing animals to known concentrations to determine the LC<sub>50</sub>, rats were exposed to essentially saturated vapours for various time periods. From vapour pressure data, MacEwen and Vernot (1977) considered that these exposures should result in calculated concentrations of approximately 1150 ppm (6611 mg/m<sup>3</sup>). Exposure of groups of five rats to saturated vapours for 4, 2 and 1 hour periods, resulted in deaths of 5, 5 and 2 rats, respectively. The rats were hyperactive early in the exposure but by 40 minutes were exhibiting tonic convulsions, tremors, and prostration. Rats that survived two or more hours of exposure were paralyzed in the posterior half of the body. Even though some of these rats survived as long as 8 days postexposure, they never regained use of this portion of the body. None of the paralyzed rats survived the 14-day postexposure observation period.

#### Probit function

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

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

with C for concentration in mg/m<sup>3</sup>.

Probit function	Species	a	b	n-value
	Rat	-32.0	4.45	N/A

Duration (min.)	LC <sub>50</sub> (mg/m <sup>3</sup> ) 95%-C.I. Male
240	4085 (2490-4770)

MacEwen and Vernot (1977) calculated a 4-hour LC<sub>50</sub> of 710 ppm (4082 mg/m<sup>3</sup>) (95% CI: 619-816 ppm (3559-4691 mg/m<sup>3</sup>)).

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



1 **Study ID: C.1**

2  
 3 **Author, year:** *MacEwen and Vernot (1977); Kinkead et al. (1992)*  
 4 Substance: Decalin  
 5 Species, strain, sex: Mouse, CF-1, female  
 6 Number/sex/conc. group: 10  
 7 Age and weight: no information  
 8 Observation period: 14 days  
 9

10 **Evaluation of study quality\***

Criteria	Comment
Study carried out according to GLP	<i>GLP did not exist at the time</i>
Study carried out according to OECD 403 guideline(s)	<i>OECD guideline 403 did not exist at the time</i>
Stability of test compound in test atmosphere	<i>No information</i>
Use of vehicle (other than air)	<i>N/A</i>
Whole body / nose-only (incl. head/nose-only) exposure	<i>Whole body</i>
Type of restrainer	<i>N/A</i>
Pressure distribution	<i>No information</i>
Homogeneity of test atmosphere in breathing zone of animals	<i>No information</i>
Number of air changes per hour	<i>Number of air changes not specified; 9 liter inhalation chamber</i>
Equilibration time (t95)	<i>Insufficient information to calculate t95</i>
Start of exposure relative to equilibration	<i>No information</i>
Actual concentration measurement	<i>Chamber concentrations were analysed using a hydrocarbon analyser</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure	<i>N/A</i>
Assessment of Reliability	<b>C</b> <i>Study limited to one exposure duration, and more importantly, study includes only two test-concentrations.</i>

11 \* Limited information concerning the study characteristics of this acute inhalation study is available.  
 12 Although this acute inhalation study was used for concentration-ranging purposes for a 30-day repeated  
 13 inhalation study, and was presented together with the results of this 30-day repeated inhalation study in a  
 14 different report, also no specific details on study characteristics were presented in this report (MacEwen  
 15 and Vernot 1978).  
 16  
 17

18 **Results**

Species	Concentration (mg/m <sup>3</sup> )		Exposure duration (min)	Lethality
	Measured	Adjusted		
				Female
				Dead/tested
Mouse	5709	N/A	240	1/10
Mouse	6238	N/A	240	5/10

19  
 20 Prior to exposing animals to known concentrations to determine the LC<sub>50</sub>, mice were  
 21 exposed to essentially saturated vapours for various time periods. From vapour

1 pressure data, MacEwen and Vernot (1977) considered that these exposures should  
2 result in calculated concentrations of approximately 1150 ppm (*6611 mg/m<sup>3</sup>*). Five of  
3 8 mice died after 4 hours exposure to saturated vapours while none of 10 died after 1  
4 hour. Symptoms were similar to the rats with tonic convulsions and tremors.  
5 However, none of the survivors showed any paralysis as was seen in the rats.

6

7 **Probit function**

8 A probit function could not be derived.

9

1 **Study ID: other C studies**

2

3 Gage (1970) exposed male and female Alderley Park rats to decalin. Exposures were  
4 performed in inhalation chambers under dynamic atmosphere conditions. The test  
5 atmosphere was prepared by injecting a liquid at a known rate into a metered stream  
6 of air by means of a controlled fluid-feed atomizer. A single 4 hour exposure to 1000  
7 ppm (5749 mg/m<sup>3</sup>) decalin resulted in mortality preceded by tremors and convulsions  
8 in 3 animals (out of total 8 animals (4m+4f)). Congestion of the lungs was reported  
9 as finding upon autopsy. Repeated (20x) 6 hour exposures to 200 ppm (1150 mg/m<sup>3</sup>)  
10 resulted in no adverse effects.

11

12 MacEwan and Vernot (1977) exposed five guinea pigs (strain and sex not specified) to  
13 375 ppm (2156 mg/m<sup>3</sup>) decalin for four hours. The guinea pigs were asymptomatic  
14 during the 4-hour exposure period and during the 14-day postexposure observation  
15 period.

16

17 Smyth et al. (1951) exposed male rats (strain not specified) for 4 hours to 500 ppm  
18 (2875 mg/m<sup>3</sup>). Four out of six animals died. In a preliminary test the maximum time  
19 for inhalation of saturated vapours (not further specified) by rats without the  
20 occurrence of deaths was 2h.

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## Appendix 2 Reference list

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