



Probit function technical support document

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substance name	CAS number
n-Butyl acetate	123-86-4

This document describes the derivation of a probit function for application in a quantitative risk analysis (QRA).

This document has been checked for completeness by the Netherlands' National Institute for Public Health and the Environment (RIVM). The contents of this document, including the probit function, have been approved by the scientific expert panel on probit functions on scientific grounds. The status of this document was therefore raised to "interim", pending a decision on its formal implementation.

Subsequently the Ministry of Infrastructure and the Environment will perform a second tier evaluation to decide whether the probit function will be formally implemented. The decision on actual implementation will primarily be based on the results of a consequence analysis.

Detailed information on the procedures for derivation, evaluation and formalization of probit functions is available at <http://www.rivm.nl/milieuportal/bibliotheek/databases/probitrelaties.jsp>.

Technical support document n-Butyl acetate

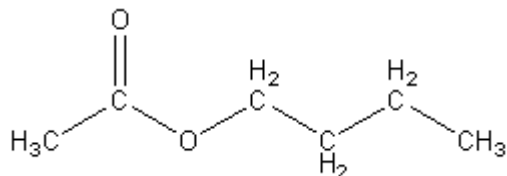
1 Substance identification

CAS-number: 123-86-4

IUPAC name: n-butyl acetate

Synonyms: Butyl acetate; butyl ethanoate; acetic acid; n-butyl ester

Molecular formula:



Molecular weight: 116.2 g/mol

Physical state: liquid (at 20°C and 101.3 kPa)

Boiling point: 126 °C (at 101.3 kPa)

Vapour pressure: 1.3 kPa (at 20°C)

Saturated vapor conc: 13,000 ppm = 62.8 g/m³ (at 20°C and 101.3 kPa)

Conversion factor: 1 mg/m³ = 0.207 ppm (at 20°C and 101.3 kPa)

1 ppm = 4.83 mg/m³ (at 20°C and 101.3 kPa)

Labelling: R10-66-67

Lower Expositive Limit 1.2 Vol% = 58,000 mg/m³

2 Mechanism of action and toxicological effects following acute exposure¹

Acute effects: The main target organs and tissues for inhalation exposure to n-butyl acetate are the respiratory tract tissues (primarily throat), conjunctiva and the central nervous system. The health endpoints are irritation to the eyes and respiratory tract (in animals and humans), and decreased motor activity, lethargy, ataxia, narcosis and death in animals. Symptoms of high exposure are lung oedema, unconsciousness and mortality. Lethality likely results from respiratory damage.

Long-term effects: Chronic exposure produces similar effects as described above. No information concerning irreversible effects is available.

3 Human toxicity data

No informative reports on lethality in humans following acute inhalation exposure were identified.

In the study by Iregren et al. (1993) three different experiments were conducted. The highest concentrations tested (i.e., 1400 mg/m³ for 20 minutes and 700 mg/m³ for four hours) elicited only minimal irritation to the eyes and respiratory tract. The physical form of exposure (vapour or aerosol) was not stated.

A human volunteer study has been described in CICADS (2005) on n-butyl acetate. Ten volunteers were exposed to 970 mg/m³ and 1400 mg/m³ for 3 to 5 minutes. The subjects reported that the lower exposure was irritating to the throat and the higher exposure concentration to be irritating to the nose and eyes and very irritating to the throat (Nelson et al., 1943; as cited in CICADS, 2005).

¹ CICADS 64, 2005 and Norris et al., 1997.

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45 **4 Animal acute toxicity data**

46 Animal lethal toxicity data considering acute exposure are described in Appendix 1. A
 47 total of 8 studies were identified -with 7 relevant datasets for 1 species- with data on
 48 lethality following acute inhalation exposure. No datasets have been assigned with
 49 status A for deriving the human probit function, 7 datasets with status B and one has
 50 been assessed to be unfit (status C) for human probit function derivation.

51 During a literature search the following technical support documents and databases
 52 have been consulted:

- 53 1. ERPG documents and reference database for n-butyl acetate, covering references
 54 before and including 1995.
- 55 2. An additional search covering publications from 1980 - 2008 was performed in
 56 HSDB, MEDline/PubMed, Toxcenter, IUCLID, RTECS, with the following
 57 search terms:
 - 58 • N-butyl acetate and synonyms
 - 59 • CAS number
 - 60 • lethal*
 - 61 • mortal*
 - 62 • fatal*
 - 63 • LC₅₀, LC
 - 64 • probit
- 65 3. Industry data were sought through networks of toxicological scientists.

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67 A total of three studies were identified in which sensory irritation was studied. In
 68 these studies the following RD₅₀ values were observed:

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<i>Species/strain</i>	<i>RD₅₀ (mg/m³)</i>	<i>Exposure duration (min)</i>	<i>Author/year</i>
Mouse / Swiss OF1	3,526	5	Muller and Greff, 1984 (as cited in ERPG 2002)
Mouse / BALB/c	8,340	Not stated	Korsak and Rydzynski, 1994 (as cited in CICADS, 2005)
Mouse / Swiss-Webster	3,550	30	Dow Chemical, UCC 1993 (as cited in ERPG 2002)

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71 **5 Probit functions**

72 It was not possible to derive a probit function for n-butyl acetate based on studies with
 73 A quality. Only one of the seven B studies allowed deriving a probit function
 74 including concentration data only for 240 minutes exposure. The probit function was
 75 derived using data from the study B.6 with B quality and listed in the table below.

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<i>Study</i>	<i>Species</i>	<i>Probit (C in mg/m³)</i>	<i>LC₅₀, 240 minutes (mg/m³)</i>

<i>ID</i>			<i>95% C.I.</i>
<i>B.6</i>	<i>Rat</i>	$-19.2 + 2.82 \times \ln C$	5,295 (3,433 – 6,228)

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6 Evaluation

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It is not possible to derive a human probit function for n-butyl acetate with sufficient reliability. The database of the acute inhalation toxicity studies for n-butyl acetate, described under appendix 1, shows inconsistent results. In three out of eight studies mortality was found, of which only one could be used to derive an 240 LC₅₀ value of 5,295 mg/m³ (Bushy Run Research Center (1993; study ID B.6). Two other studies, Bushy Run Research Center (1987; study ID B.5) and NOTOX (1986; C study) also found mortalities, but the calculated LC₅₀ values was either based on two exposures resulting in 0 and 100% mortality or was lower than the concentrations tested in the study.

In several other studies, at exposure concentrations far exceeding the concentrations of the abovementioned studies where mortalities were observed, all animals survived. All available studies were given the B-status, because the studies were well performed and documented. Since only one duration was considered the studies were deprived the A-status.

No clear explanations could be found for this inconsistency in the results, although attempts were made (ERPG, 2002; Norris et al., 1997) to rule out possible exposure factors such as vapour generation methods and whole body versus head/nose-only exposure. A possible explanation for the inconsistencies might be the presence of impurities in the old production batches. That might explain the mortality observed in some of the studies. However, based on the available data, no definite conclusions can be drawn on this point.

If we were to ignore the inconsistency of the data and use the 240 LC₅₀ value of 5,295 mg/m³ (Bushy Run Research Center (1993; study ID B.6) as point of departure for the human probit function (see appendix 2); lethal concentrations will be derived that are approximately at the same level and even below the concentrations used in the two human volunteer studies (see section 3). In the volunteer studies only irritation of the nose, eyes and respiratory tract were noted.

Other guideline levels, such as the ERPG-3 (15,000 mg/m³) and the LBW (10,000 mg/m³) use a repeated dose toxicity study as point of departure. Rats were exposed at 15,000 mg/m³ n-butyl acetate for 6h/d 5d/week for 14 weeks. No mortalities were observed during the study (David et al., 1998).

For the abovementioned reasons the studies that reported mortality are not suitable for derivation of a human probit function since such a function would conflict with other animal and human data. Since mortality data is lacking in other studies, it is concluded that no human probit function for n-butyl acetate can be derived with sufficient reliability.

124 **Appendix 1 Animal experimental research**

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126 **Study ID: B.1**

127 **Author, year: BASF, 1988a**

128 Substance: n-butyl acetate

129 Species, strain, sex: Male and female Wistar rats

130 Number/sex/concentration group: 5/sex per group

131 Age and weight: Males: 258 g and females: 189 g aged 8-9 weeks.

132 Observation period: 14 days

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<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403</i>
Stability of test compound in test atmosphere	<i>No information.</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Head/nose-only</i>
Pressure distribution.	<i>By means of an exhaust system the pressure ratios were adjusted in such way that the amount of exhaust air was about 1/3 lower. This prohibits dilution of the test substance with laboratory air.</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>A liquid aerosol was generated by means of a continuous infusion pump and a 2-component atomizer.</i>
Number of air changes per hour	<i>600 l/h (compressed air)</i>
Actual concentration measurement	<i>Gas chromatography (GC) was used to analyze the atmosphere. Location was immediately adjacent to the animals' noses. One sample about hourly.</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>Measured by means of 1) collecting disks followed by GC and 2) light scattering photometer. No particles detected.</i>
Assessment of Reliability	<i>B, well conducted study, however the study includes only one exposure concentration that did not result in mortality.</i>

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136 **Results**

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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rat	21,100	240	0/5	0/5

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141 **Probit function**

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143 A probit function could not be derived based on the data by BASF 1988a.

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146 **Study ID: B.2**
 147 **Author, year: BASF 1988b**
 148 Substance: n-butyl acetate
 149 Species, strain, sex: Male and female wistar rats
 150 Number/sex/concentration group: 5/sex per group.
 151 Age and weight: Males 271 g, Females 197 g, aged 8-9 weeks.
 152 Observation period: 14 days.
 153

<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403</i>
Stability of test compound in test atmosphere	<i>No information.</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Head/nose-only</i>
Pressure distribution.	<i>By means of an exhaust system the pressure ratios were adjusted in such way that the amount of exhaust air was about 10% lower. This prohibits dilution of the test substance with laboratory air.</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>A vapour was generated by means of a continuous infusion pump and a glass vaporizer with thermostat (evaporation by heating).</i>
Number of air changes per hour	<i>1500 l/h</i>
Actual concentration measurement	<i>Gas chromatography (GC) was used to analyze the atmosphere. Location was immediately adjacent to the animals' noses. One sample about hourly.</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>A quartz wool plug was used as aerosol barrier. Particle detection was not performed.</i>
Assessment of Reliability	<i>B, well conducted study, however the study includes only one exposure concentration, which did not result in mortality.</i>

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156 **Results**

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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rat	21,000	240	0/5	0/5

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161 **Probit function**

162 A probit function could not be derived based on the data by BASF 1988b.

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167 **Study ID: B.3**
 168 **Author, year: NOTOX 1988 (sponsored by BASF)**
 169 Substance: n-butyl acetate
 170 Species, strain, sex: Male and Female Wistar rats
 171 Number/sex/concentration group: 5 / sex / concentration
 172 Age and weight: males 302 g, females 215 g. Aged 8 weeks
 173 Observation period: 14 days
 174

<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403 EEC Directive 84/449/EEC. Annex V of Directive 67/548/EEC</i>
Stability of test compound in test atmosphere	<i>No information.</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Head-only</i>
Pressure distribution.	<i>Positive pressure at the nose of the animals (central cylinder), negative pressure in surrounding hood.</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>A dynamic spraying nozzle was used to generate the test substance. The substance is delivered by an infusion pump.</i>
Number of air changes per hour	<i>10 l/min</i>
Actual concentration measurement	<i>Chamber atmosphere was sampled at the same level as the breathing orifices. Samples were taken hourly and analyzed by gas chromatography.</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>Sampling of test atmosphere with a low pressure cascade impactor close to the breathing zone of the animals. Main part was present as vapour rather than as an aerosol.</i>
Assessment of Reliability	<i>B</i> , well conducted study, however the study includes only one exposure concentration that did not result in mortality.

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183 **Results**

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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rat	4,900	240	0/5	0/5

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187 **Probit function**

188 A probit function could not be derived based on the data by NOTOX 1988

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191 **Study ID: B.4**
 192 **Author, year: BASF 1988c**
 193 Substance: n-butyl acetate
 194 Species, strain, sex: male and female Wistar rats
 195 Number/sex/concentration group: 5 / sex / concentration
 196 Age and weight: male 299 g and female 196 g. Aged 8-9 weeks.
 197 Observation period: 14 days
 198

<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403</i>
Stability of test compound in test atmosphere	<i>No information</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Head/nose-only</i>
Pressure distribution.	<i>By means of an exhaust system the pressure ratios were adjusted in such way that the amount of exhaust air was about 10% lower. This prohibits dilution of the test substance with laboratory air.</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>A liquid aerosol was generated by means of a continuous infusion pump and a 2-component atomizer.</i>
Number of air changes per hour	<i>1500 l/h (compressed air)</i>
Actual concentration measurement	<i>Gas chromatography (GC) was used to analyze the atmosphere. Location was immediately adjacent to the animals' noses. One sample about hourly.</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>Measured by means of metal collecting disks in the impactor followed by GC. No aerosol particles were detectable.</i>
Assessment of Reliability	<i>B</i> , well conducted study, however the study includes only two exposure concentrations that did not result in mortality.

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Results

Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rat	1,970	240	0/5	0/5
	23,400	240	0/5	0/5

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205 **Probit function**

206 A probit function could not be derived based on the data by BASF 1988c.

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209 **Study ID: B.5**
 210 **Author, year: Bushy Run Research Center (1987; sponsored by Union**
 211 **Carbide Cooperation)**
 212 Substance: n-butyl acetate
 213 Species, strain, sex: Male and female Sprague-Dawley albino rats
 214 Number/sex/concentration group: 5/sex/group, 6 groups in total.
 215 Age and weight: 50-62 days of age, weights ranged from 157 - 214 g (female) and
 216 199 to 290 g (male). Exact weights given per animal individually and per sex/group.
 217 Observation period: 14 days
 218

<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Compliance with OECD/TSCA/FIFRA GLP</i>
Study carried out according to guideline(s)	<i>No information</i>
Stability of test compound in test atmosphere	<i>Using the atomizer for vapour generation resulted in aerosol formation</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Whole body</i>
Pressure distribution.	<i>No information</i>
Homogeneity of test atmosphere at breathing zone of animals	<p><i>n-Butyl acetate test atmosphere was generated in three different ways: statically, dynamically by using a evaporator and dynamically by using an atomizer.</i></p> <ol style="list-style-type: none"> <i>1. Static exposure: test material was placed in an open tray at the top of a sealed 120 l chamber. Vapours were allowed to achieve equilibrium after 17 hours after which the animals were placed into the chamber.</i> <i>2. Dynamically by evaporation: test material was metered with a pump into a heated evaporator. The vapour mixture was carried to the chamber using a countercurrent air stream that entered the bottom of the evaporator.</i> <i>3. A metered amount of test material was introduced to a atomizer with a liquid and air nozzle. The atomizer was placed at the top of the chamber. Liquid aerosol/vapour was diluted to the desired vapour concentration and dispersed throughout the chamber by filtered supply air.</i>

Number of air changes per hour	<p>1) <i>static</i></p> <p>2) <i>200 l/min gives 13.3 air changes per hour (900 l chamber)</i></p> <p>3) <i>250 to 300 l/min gives 11.5 to 13.8 air changes per hour (1300 l chamber)</i></p>
Actual concentration measurement	<i>Concentrations were measured by gas chromatography at least 10 times during the 4h exposure period. The analytical/nominal ratios ranged from 0.88 to 0.92.</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>Not determined.</i>
Assessment of Reliability	<i>B</i> <i>Well conducted study that included six concentration groups divided over three vapour generation methods. One exposure duration was considered. Data not suitable for probit function derivation.</i>

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Results

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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rats	33,168 (static)	240	0/5	0/5
	30,598 (evaporator)	240	0/5	0/5
	14,553 (evaporator)	240	0/5	0/5
	9,790 (evaporator)	240	0/5	0/5
	2,608 (atomizer)	240	5/5	5/5
	1,367 (atomizer)	240	0/5	0/5

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Probit function

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Based on the data it was not possible to derive a probit function. The author stated a 4h LC₅₀ value of 1,889 mg/m³ for male and female rats with a confidence interval (95%) of 1,425 to 2,497 mg/m³.

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229 **Study ID: B.6**
 230 **Author, year: Bushy Run Research Center (1993; sponsored by Union**
 231 **Carbide Coorporation)**
 232 Substance: n-butyl acetate
 233 Species, strain, sex: Male and female Sprague-Dawley albino rats
 234 Number/sex/concentration group: 5/sex/group, 4 groups in total.
 235 Age and weight: Weights ranged 218 to 290 g (males) and 172 to 213 g (females)
 236 Observation period: 14 days
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<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403</i>
Stability of test compound in test atmosphere	<i>Author indicates that aerosol formation occurred during exposure.</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Whole body</i>
Pressure distribution.	<i>No information</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>Test substance was metered from a pump into an atomizer fitted with a liquid and air nozzle. The atomizer was positioned at the top of the chamber where the aerosol was generated. Either filtered air or dry compressed cylinder air (6,004 mg/m³) was passed through the atomizer.</i>
Number of air changes per hour	<i>12 to 17 air changes per hour</i>
Actual concentration measurement	<i>Concentrations were measured using gas chromatography, equipped with a flame ionization detector, 9 to 16 times</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>The particle size distribution was measured using a TSI aerodynamic Particle Sizer Model (for two exposure groups). Mass Median Aerodynamic Diameters were 1.34 and 2.03 microns in groups 6,004 mg/m³ and 6,066 mg/m³, respectively. Particles were present in very low amounts compared to the vapour</i>
Assessment of Reliability	<i>B</i> <i>Well conducted study. Only one exposure duration was included.</i>

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240 **Results**

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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rats	4,178	240	1/5	2/5
	6,004	240	2/5	3/5
	6,066	240	4/5	2/5
	6,873	240	5/5	4/5

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245 **Probit function**

246 The probit function and associated LC-values have been calculated using the

247 DoseResp program by Wil ten Berge (version December 2006) as

248 $Pr = a + b \times \ln C + d \times S$ 249 with C for concentration in mg/m³, S for sex (0 = female, 1 = male).

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<i>Probit function</i>	<i>Species</i>	<i>a</i>	<i>b</i>	<i>d</i>
Sex as covariate	<i>Rat</i>	-19.3	2.82	0.15
Sexes combined	<i>Rat</i>	-19.2	2.82	

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<i>Duration (minutes)</i>	<i>LC₅₀ (mg/m³) 95%-C.I. Male</i>	<i>LC₅₀ (mg/m³) 95%-C.I. Female</i>	<i>LC₅₀ (mg/m³) 95%-C.I. Combined</i>
240	5,155 (2,865 – 6,532)	5,428 (3,408 – 7,100)	5,295 (3,433 – 6,228)

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256 **Study ID: B.7**
 257 **Author, year: Bushy Run Research Center (1994; sponsored by Union**
 258 **Carbide Cooperation)**
 259 Substance: n-butyl acetate
 260 Species, strain, sex: Male and female Sprague-Dawley albino rats
 261 Number/sex/concentration group: 5/sex/group, 9 groups in total.
 262 Age and weight: Weights ranged 180 to 296 g (males) and 140 to 210 g (females)
 263 Observation period: 14 days
 264

<i>Criteria</i>	<i>Comment</i>
Study carried out according to GLP	<i>Yes</i>
Study carried out according to guideline(s)	<i>OECD guideline 403</i>
Stability of test compound in test atmosphere	<i>Author indicates that aerosol formation occurred during exposure.</i>
Use of vehicle (other than air)	
Whole body / nose-only (incl. head/nose-only) exposure	<i>Whole body</i>
Pressure distribution.	<i>No information</i>
Homogeneity of test atmosphere at breathing zone of animals	<i>Test substance was metered from a pump into an atomizer (three different types were used) fitted with a liquid and air nozzle. The atomizer was positioned at the top of the chamber where the aerosol was generated. In two exposure groups the filtered air was conditioned to 100% relative humidity.</i>
Number of air changes per hour	<i>14 air changes per hour</i>
Actual concentration measurement	<i>Concentrations were measured using gas chromatography, equipped with a flame ionization detector, 14 to 21 times</i>
Particle size distribution measurement in breathing zone of the animals in case of aerosol exposure;	<i>The particle size distribution was measured using a TSI aerodynamic Particle Sizer Model. Mass Median Aerodynamic Diameters ranged from 0.79 to 2.68 microns. In addition, submicron particles were measured using a TSI Condensation Particle Counter. Submicron particles amounts ranged from 1.56×10^5 to 22.5×10^5 particles/cc.</i>
Assessment of Reliability	<i>B</i> <i>Well conducted study, however none of the exposures resulted in mortality.</i>

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267 **Results**
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Species	Concentration (mg/m ³)	Exposure duration (min)	Lethality	
			Male	Female
Rats	3,854	240	0/5	0/5
	6,815	240	0/5	0/5
	6,965 ^a	240	0/5	0/5
	7,313 ^b	240	0/5	0/5
	7,327 ^c	240	0/5	0/5
	7,482 ^d	240	0/5	0/5
	7,607 ^e	240	0/5	0/5
	24,546	240	0/5	0/5
	44,977	240	0/5	0/5

270 ^a: exposure with relative humidity of 52% and 20 psi operation pressure of atomizer.

271 ^b: exposure with relative humidity of 38% and 30 psi operation pressure of atomizer,
 272 using another batch of n-butyl acetate.

273 ^c: exposure with relative humidity of 100% and 20 psi operation pressure of atomizer.

274 ^d: exposure with relative humidity of 100% and 20 psi operation pressure of atomizer,
 275 using another batch of n-butyl acetate.

276 ^e: exposure with relative humidity of 46% and 20 psi operation pressure of atomizer.

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279 **Probit function**

280 Deriving a probit function based on these data is not possible.

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282 ***Other studies (C quality)***

283 In an article by Norris et al., (1997) abovementioned studies are described with the addition of
284 an eighth study performed by NOTOX in 1986 (sponsored by 3M UK). The original study
285 report was not available.

286 Wistar rats were exposed to aerosolized n-butyl acetate in a dynamic spraying head-only
287 exposure system. Five rats/sex/group were exposed to 815, 2,241 and 5,296 mg/m³ for 4
288 hours and observed for 14 days postexposure. The mass median aerodynamic diameter was
289 1.01 micron with a geometric standard deviation of 3.30. Lethality of the sexes combined
290 were 60, 100 and 100% for 815, 2,241 and 5,296 mg/m³, respectively. The calculated LC₅₀
291 value was 773 mg/m³ with a 95% confidence interval of 584 to 1,024 mg/m³.

292 **Appendix 2 Human probit function based on study B.6.**

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294 As point of departure for deriving the human probit function the 240 min LC₅₀ value
 295 of **5,295 mg/m³** for the rat was taken. The human equivalent LC₅₀ was calculated by
 296 applying the following assessment factors:

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Assessment factor for:	Factor	Rationale
Animal to human extrapolation:	3	
RD ₅₀	1	RD ₅₀ is less than a factor 2 below the LC ₅₀ .
Nominal concentration	1	Analytical concentrations were used.
Adequacy of database:	1	Large dataset including well conducted studies. A conservative approach was applied since other studies observed no mortality at higher concentrations than the LC ₅₀ values used as point of departure.

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299 The estimated human equivalent 240-minute LC₅₀ value is $5,295 / 3 = \mathbf{1,765 \text{ mg/m}^3}$.

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301 The n-value was set at **2 as default**. Assuming a regression coefficient (b×n) of 2 for
 302 the slope of the curve, the b-value can be calculated as $2 / n = \mathbf{1}$.

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304 The human probit function is then calculated on the human equivalent 240 min LC₅₀
 305 and using the above parameters to solve the following equation to obtain the a-value
 306 (the intercept): $5 = a + 1 \times \ln (1,054^2 \times 240)$ resulting in the a-value of **-15.43**.

307

308 **Pr = -15.4 + 1 × ln (C² × t)** with C in mg/m³ and t in min.

309

310 The derived human probit function has a scientifically weak basis. The probit function
 311 is based on one study in the rat with B quality, where 5 animals/sex/group were
 312 exposed to four different concentrations for 4 hours. Because there are major
 313 inconsistencies in the total dataset for n-butyl acetate the basis for this probit function
 314 is considered weak.

315

316 The human 60 min LC₁ (Pr = 2.67) calculated with this probit equation is 1,085
 317 mg/m³ and the calculated human 60 min LC_{0.1} (Pr = 1.93) is 741 mg/m³.

318

Estimated level	30 min (mg/m ³)	60 min (mg/m ³)
1% lethality, this probit	1,535	1,085
0.1% lethality, this probit	1,048	741
AEGL-3	-	-
ERPG-3 (2002)		14,490
LBW (2007)		10,000

319

320 Comparing to equivalent (inter)national guideline levels as presented in the table
 321 above, the derived lethality estimates using the probit function above are not in

322 agreement. The reason is that the ERPG based its value on reported concentrations
323 that did not result in mortality in animals and did not include the Bushy Run Research
324 Center (1993; study ID B.6) study in their document. The ERPG also failed to report
325 the mortality observed in the Bushy Run Research Center (1987; study ID B.5),
326 whereas indeed the other data was reported.

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