Liquefied petroleum gas (LPG)
(CAS No: 68476-85-7)

Propane
(CAS No: 74-98-6)

Butane
(CAS No: 106-97-8)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

No. 2000/15OSH/134 The Hague, November 9, 2004

all rights reserved
1 Introduction

The present document contains the assessment of the health hazard of liquefied petroleum gas (LPG) and its components butane and propane by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. First drafts of separate documents on LPG and butane were prepared by MA Maclaine Pont, M.Sc. (Wageningen University and Research Centre, Wageningen, the Netherlands) and AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands), respectively.

The evaluation of the toxicity of butane and propane has been based on the reviews by Berzins (Ber95a, Ber95b) and Low et al. (Low87a, Low87b). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, in February 1998, literature was searched on the databases Medline, Toxline, and Chemical Abstracts, starting from 1966, 1981, and 1937, respectively, and using the following key words: liquefied petroleum gas, LPG, propane, butane, butylhydride, 68476-85-7, 74-98-6, and 106-97-8. Data on intoxication from combustion products were excluded from the document.

In March 2000, the President of the Health Council released separate drafts of documents on butane and LPG for public review. Comments were received from the following individuals and organisations: A Aalto (Ministry of Social Affairs and Health, Tampere, Finland), JH Urbanus (CONCAWE, Brussels, Belgium), P Wardenbach, Ph.D. (Bundesanstalt für Arbeitsschutz and Arbeitsmedizin, Dortmund, FRG), and L Whitford (Health and Safety Executive, London, England). These comments were taken into account when deciding on the final version of the document*.

An additional search in Toxline and Medline in April 2004 did not result in information changing the committee’s conclusions.

* In the finalising phase, it was decided to combine the documents on LPG (including propane) and butane into one document.
2 Identity

name: liquefied petroleum gas propane butane
synonyms: LPG; petroleum gas; n-propane; dimethylmethane; propyl hydride; propyl dihydride; n-butane; butylhydride; methylethylmethane; diethyl
molecular formula: C₃H₈ C₄H₁₀
structural formula: CH₃-CH₂-CH₃ CH₃-CH₂-CH₂-CH₃
CAS number: 68476-85-7* 74-98-6 106-97-8

* CAS does not treat this substance as a unique chemical entity in its regular CA index processing.

3 Physical and chemical properties

<table>
<thead>
<tr>
<th></th>
<th>LPG</th>
<th>propane</th>
<th>n-butane</th>
</tr>
</thead>
<tbody>
<tr>
<td>molecular weight</td>
<td>42-58</td>
<td>44.09</td>
<td>58.12</td>
</tr>
<tr>
<td>boiling point</td>
<td>-44°C</td>
<td>-42.1°C</td>
<td>-0.5°C</td>
</tr>
<tr>
<td>melting point</td>
<td>not available</td>
<td>-189.7°C</td>
<td>-138.2°C</td>
</tr>
<tr>
<td>flash point</td>
<td>not found</td>
<td>-104°C (closed cup)</td>
<td>-60°C (closed cup)</td>
</tr>
<tr>
<td>vapour pressure</td>
<td>&gt;100 kPa</td>
<td>at 21°C: 853 kPa</td>
<td>at 25°C: 243 kPa</td>
</tr>
<tr>
<td>solubility in water</td>
<td>insoluble</td>
<td>insoluble</td>
<td>insoluble</td>
</tr>
<tr>
<td>log P&lt;sub&gt;octanol/water&lt;/sub&gt;</td>
<td>not available</td>
<td>2.36 (experimental)</td>
<td>2.89 (experimental)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.81 (calculated)</td>
<td>2.31 (calculated)</td>
</tr>
<tr>
<td>conversion factors</td>
<td>at 20°C, 101.3 kPa:</td>
<td>at 20°C, 101.3 kPa:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 mg/m³ = 0.54 ppm</td>
<td>1 mg/m³ = 0.41 ppm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 ppm = 1.84 mg/m³</td>
<td>1 ppm = 2.42 mg/m³</td>
<td></td>
</tr>
</tbody>
</table>

Data from ACG02a, ACG02b, ACG02c, Ber95a, Ber95b, CON92, NLM04a, NLM04b, http://www.syres.com/esc/est_kowdemo.htm.

LPG

LPG is a by-product of petroleum refining. It is a colourless gas with a mild odour. An odour threshold ranging from 5000-20,000 ppm has been reported. A foul odorant (e.g., ethanethiol) is added commercially. LPG is highly flammable and is a dangerous fire and explosive hazard (ACG02a).

LPG is commercially available as propane (often found in colder climates), butane (more widely found in the Southern States of the USA due to its higher freezing and boiling points), and butane-propane mixtures (ACG02a). Others state that LPG is predominantly a mixture of C₃ and C₄ hydrocarbons with other hydrocarbons in the C₁-C₇ range. These are gases at normal ambient temperatures and pressures (CON92). In the Netherlands, LPG is blended by the Shell Company mainly from propane/propene and butane/butene refinery streams, both streams consisting for >90% of C₃ or C₄ molecules, respectively.
The proportion of longer chain molecules ($\geq C_5$) is 2% at most; the share of the unsaturated molecules is approximately 30%. The boiling point ranges from -40 to +40°C (Kat98).

**Propane**
Propane is a colourless and odourless flammable gas (Ber95a). Amoore and Hautala listed an odour threshold for propane of 16,000 ppm (29,440 mg/m$^3$) (Amo83) while Ruth reported the odour threshold to range between 972 and 19,440 ppm (1800 and 36,000 mg/m$^3$) (Rut86).

**Butane**
Butane is a colourless and flammable gas with a gasoline-like or natural gas odour (ACG02c). Amoore and Hautala listed an odour threshold for butane of 2700 ppm (6530 mg/m$^3$) (Amo83) while Ruth reported the odour threshold to range between 1.2 and 6 ppm (2.9 and 14.6 mg/m$^3$) (Rut86).

### Uses

**LPG**
LPGs are widely used as fuel and as feedstock in chemical processes. In some countries, there is also extensive use of LPG as automotive fuel. LPGs are also used as propellants in pressurised aerosol containers (CON92).

**Propane**
Propane is used as fuel gas in the household, industry, and vehicles (sometimes mixed with butane), in organic synthesis, as an intermediate in petrochemical manufacture, as a refrigerant and aerosol propellant (amongst others in cosmetics). It occurs in natural gas (Ber95a, Moo82). In the USA, it has a GRAS (‘generally recognised as safe’) status for use as a food additive, i.e., to expel a product or to reduce the amount of oxygen in contact with the food in the packaging (see Code of Federal Regulations: 21CFR184.1165; revised as of April 1, 2003).

**Butane**
Butane is used in liquid fuels of high octane, in organic synthesis of different chemicals, in the production of synthetic rubbers, as a refrigerant and aerosol propellant (amongst others in cosmetics), and as a constituent in liquid natural gas (Ber95b, Moo82). In the USA, it has a GRAS (‘generally recognised as safe’) status for use as a food additive, i.e., to expel a product or to reduce the
amount of oxygen in contact with the food in the packaging (see Code of Federal Regulations: 21CFR184.1165; revised as of April 1, 2003).

5 Biotransformation and kinetics

LPG
In male ICR mice exposed to an unknown concentration of LPG (composition: 97.4% propane, 0.3% butane, 1.2% ethane, and 1.1% 2-methylpropane) for 2 hours, propane, butane, and 2-methylpropane and the metabolites 2-propanol, acetone, 2-butanol, and 2-butanone were identified in blood, brain, liver, and kidneys (Tsu85a).

Propane
One hour after inhalation of an unknown concentration of propane, unchanged compound was detected in blood, brain, liver, and kidneys of male ICR mice. 2-Propanol and acetone, metabolites of propane, were also identified. Following incubation of a saturated aqueous solution of propane (ca. 2.9 mM) with a mouse liver microsomal suspension in the presence of a NADPH-generating system, Tsukamoto et al. only found 2-propanol, while no ketone was detected. From these data, the authors presumed that propane was first metabolised into a secondary alcohol, 2-propanol, by the microsomal enzyme system and then into the corresponding ketone, acetone, by alcohol dehydrogenase (Tsu85a, Tsu85b).

Propane has been detected in blood, brain, kidney, liver, and lungs of man following fatal propane exposure (Ber95a, Gra99).

Butane
In humans, absorption of butane was reported to be 30-45% of the dose inhaled (Fla90). Although the committee did not find data on absorption through the skin, dermal penetration of butane is expected to be low since skin contact is transient due to the volatility of the compound (Low87b).

In a fatal case of butane abuse, levels of butane in liver, brain, blood, and kidneys amounted to 310, 282, 129, and 84 mg/kg or mg/L, respectively (Gra99).

In rats exposed to a butane concentration of 100 ppm (240 mg/m³) for 80 minutes, the uptake was estimated to be 1.5-1.8 nmol/kg/min/ppm (0.09-0.1 µg/kg/min/ppm) (Dah88). From this, a retention of ca. 10% can be calculated (assuming a rat body weight of 300 g and a minute volume of 125 mL/min).
Butane is distributed to various tissues. After exposing rats to lethal concentrations of ca. 650,000 mg/m³ (ca. 270,000 ppm) for 4 hours, Shugaev found the highest concentration of butane in the perirenal fat tissue, followed by the brain, spleen, liver, and kidney (Shu69).

One hour after inhalation to an unknown concentration of butane, unchanged compound was detected in blood, brain, liver, and kidneys of male ICR mice. 2-Butanol and 2-butanone, metabolites of butane, were also identified. As with propane (see above), incubation of a saturated aqueous solution of butane (ca. 6.7 mM) with a mouse liver microsomal suspension in the presence of a NADPH-generating system, only 2-butanol, but no ketone was detected. Tsukamoto proposed a metabolism scheme similar to that described above for propane (Tsu85a, Tsu85b).

Low et al. reported that in rat liver microsomes, butane was hydroxylated yielding 2-butanol as the major metabolite. Butane was the lowest molecular weight alkane demonstrated to bind as a substrate to cytochrome P450. The authors suggested that if 2-butanol would be the major metabolite formed in mammals, it could be excreted in exhaled air. Like other alcoholic metabolites formed from hydroxylation of normal alkanes, 2-butanol may also be conjugated with glucuronic acid or be oxidised into methyl ethyl ketone, which could be expired as well (Low87b).

Because of its volatile nature, unchanged butane may also be exhaled, and its determination in exhaled air might be used for biological monitoring purposes.

### 6 Effects and mechanism of action

#### Human data

**LPG**

A few cases on death following accidental or intentional inhalation of LPG have been reported (Kir92, Fuk96). Aydin and Özçakar described a case of a 28-year-old man complaining of nausea, malaise, and generalised weakness of the lower limbs. The patient was hospitalised with a diagnosis of suspected acute hepatitis that was attributed to have been working in an enclosed space fixing gas cylinders containing a propane-butane mixture (Ayd03). Abnormal liver function and neurological symptoms were found in a 63-year-old man after inhaling a mixture containing propane, butane, and 2-methylpropane (30-35%), but also petroleum distillates 25-35%), pentane (10-15%), and acetone (1-5%). The symptoms subsided after discontinuation of exposure (Pya98).
Propane
At very high levels, propane has CNS depressant and asphyxiating properties. Several cases of fatal inhalation of propane have been described (Avi94, Gra99, Sie90, Tso98; see also Ber95a, Cav94). Bowen et al. reported that out of 52 deaths associated with accidental or intentional inhalation of volatile compounds in Virginia (USA) in the period 1987-1996, 6 cases were due to suicide and 7 to accidental overexposure in, usually, the workplace, but the compounds involved were not specified. Of the remaining 39 cases in which death was considered to be a direct consequence of inhalant abuse, 5 were associated with propane (Bow99).

A 17-year-old male reported feelings of euphoria, ataxia, and light-headedness without loss of consciousness when inhaling propane intentionally for 10-15 seconds and subsequently holding his breath for up to one minute. These sensations lasted for 1-2 minutes. This inhalation pattern would be repeated daily for periods up to 3 hours for 6 months. The man complained of severe headache and memory loss on the morning after exposure. Physical examination, including a neurological assessment, and laboratory tests (complete blood count with differential, blood urea nitrogen, serum creatinine, electrolytes, routine urinalysis, liver function tests) did not reveal abnormalities (Whe92).

Several cases of cold injury from liquid propane have been published. The injuries were similar to frostbite but the symptoms occurred more rapidly with propane (Ber95a).

No changes in EEGs, adrenocortical functions, pulmonary functions, neurological response, subjective response, cardiac function, cognitive response, or visual evoked response were seen in 8 men and women exposed to propane concentrations of 250 and 1000 ppm (460 and 1840 mg/m³) for 1 minute to 8 hours or in 2 men and 2 women exposed to 1000 ppm (1840 mg/m³) propane, 8 hours/day for 5 consecutive days at one week and 4 consecutive days the following week (Ber95a, Low87a, Moo82).

Ten-minute exposures to 10,000 ppm (18,400 mg/m³) did not produce symptoms in 6 men and women; distinct vertigo, but no mucosal irritation of nose, eyes, or respiratory tract, was observed at exposures to up to 100,000 ppm (184,000 mg/m³) for 2 minutes (Moo82).

Assuming a correlation between the anaesthetic potency of a gas and its air/olive oil partition coefficient, Drummond expected that a concentration of propane of 47,000 ppm (86,500 mg/m³) would induce narcosis in man (Dru93).
Butane

Several individual cases or retrospective studies (in e.g., England, Germany, and the USA) in which butane was identified as the toxic agent have been reported. They mostly concern its abuse as an inhalant, from, e.g., lighters or hair/deodorant sprays, by teenagers and adolescents. Butane abuse was fatal, mostly due to heart failure (arrhythmias, ventricular fibrillation, asystole) (Bla98, Bow99, Cha02, Dör02, Fie03, Gra99, Rob90, Roh97, Weh02, Wil98) and, in one case, due to multiple organ failure involving the central nervous system, cardiovascular system, pulmonary system, and the liver (Rie00). Bowen et al. reported that out of 52 deaths associated with accidental or intentional inhalation of volatile compounds in Virginia (USA) in the period 1987-1996, 6 cases were due to suicide and 7 to accidental overexposure in, usually, the workplace, but the compounds involved were not specified. Of the remaining 39 cases in which death was considered to be a direct consequence of inhalant abuse, 13 were associated with butane (Bow99). Butane induced severe acute neurological (seizure, somnolence, coma) or cardiovascular (ventricular fibrillation, asystole, collapse) complications and minor symptoms such as nausea, dizziness, vomiting, headache, and sore throat (Dör02, Edw00, ONe99). Döring et al. described a case of severe encephalopathy in a 15-year-old girl having inhaled butane repeatedly for 4 weeks when an acute abuse incident occurred. After admittance to the hospital, involving cardiopulmonary resuscitation, 6-day catecholamine treatment, and 11-day mechanic ventilation, severe brain damage with vigil coma and spastic quadriplegia became obvious during the following weeks. Repetitive MRI-imaging revealed disintegration of grey matter, increasing cerebral atrophy, and destruction of basal ganglia while EEG showed strongly diminished basal activity with flat amplitude (Dör02). Gray and Lazarus presented a case of a right-sided hemiparesis characterised by markedly reduced power - grade 1/5 - in the right arm and leg, flaccid tone, and absent reflexes with an extensor plantar reflex on this side (Gra93). Frangides et al. reported a (very rare) case of non-fatal acute massive rhabdomyolysis in a 27-year-old man due to accidental inhalation of liquid gas fumes leaking from a tank containing a mixture of butane (80%), propane (20%), ethanethiol, and olefines (Fra03). McIntyre and Long concluded that fulminant hepatic failure after taking a proprietary engine or carburettor cleaner, containing isopropyl alcohol, mineral oil, and aromatic petroleum products, was the cause of death of a 17-year-old male having been abusing butane aerosols for 3 years (McI92).

Two cases of pregnant women accidentally (in pregnancy week 27) or intentionally (suicide attempt in week 30) were reported. The first woman gave birth to a child with hydranencephaly (Fer86), while the second woman gave
birth to a child that died after 11 hours with severe encephalomalacia and hypoplastic kidneys (Gos82). In both cases, these brain effects were not considered to be a butane-specific effect but to have been caused by intrauterine anoxia. In neither of these cases, estimations of the concentrations inhaled were made.

Viau et al. did not find clinically significant effects on sensitive biochemical and immunological markers of kidney (functioning) in 53 male refinery workers who were occupationally exposed for an average of 11 years to a number of hydrocarbons, among which butane (concentration ranged from 0.4 to 17.8 mg/m³) (Via87).

In human subjects exposed to a butane concentration of 10,000 ppm (24,200 mg/m³) for 10 minutes, drowsiness was reported (no more data presented) (Low87b, Moo82).

Assuming a correlation between the anaesthetic potency of a gas and its air/olive oil partition coefficient, Drummond expected that a concentration of butane of 17,000 ppm (40,290 mg/m³) would induce narcosis in man (Dru93).

Animal data

**LPG**
The committee did not find data from experimental animal studies with LPG.

**Propane**
The committee did not find data on the irritating properties of propane or of formulations containing propane only. Applications of several formulations containing 63-69% 2-methylpropane and 12-13% propane to the clipped back skin of rabbits resulted in primary irritation index scores of 0.38-0.73 (maximum possible score: 8.0) (Moo82).

In guinea pigs, irregular breathing or tremors (during the first 5 minutes) were observed at 5-120 minute exposures to ca. 44,000-53,000 (24,000-29,000 ppm) or 86,000-101,000 mg/m³ (47,000-55,000 ppm), respectively. Nausea, retching, and stupefaction were seen at longer exposure durations; narcotic effects not until exposure levels were ca. 92,000 mg/m³ (50,000 ppm). No mortality or pathological changes were observed (Low87a). The EC₅₀ for effects on the central nervous system (ataxia and loss of righting reflex) in rats was ca. 52,000 mg/m³ (28,000 ppm) (exposure time: 10 minutes) (Cla82). When propane was administered by tracheal cannula to anaesthetised rhesus monkeys (n=3/group) at concentrations of ca. 180,000 and 360,000 mg/m³ (100,000 or 200,000 ppm), for 5 minutes followed by inhalation of room air for 10 minutes, it induced
increases (not statistically significant: p>0.05) in bronchoconstriction and respiratory depression at the high level, but no arrhythmia or myocardial depression (Bel74, Avi75). In anaesthetised mice and unanaesthetised dogs, propane did not induce arrhythmias either but (weakly) sensitised the heart to epinephrine-induced cardiac arrhythmias at concentrations of ca. 180,000 and 360,000 mg/m$^3$ (100,000 and 200,000 ppm), but in dogs not at ca. 90,000 mg/m$^3$ or 50,000 ppm (exposure time: mice: 6 minutes; dogs: 10 minutes) (Avi74, Rei71). Similar effects were observed in dogs exposed to concentrations of ca. 280,000 to 1,656,000 mg/m$^3$ (150,000-900,000 ppm) for 10 minutes (Low87a). In another study, propane was a weak cardiac sensitiser in dogs: the EC$_{50}$ was ca. 33,000 mg/m$^3$ (18,000 ppm) (exposure time: 5 minutes) (Cla82).

The committee did not find data from repeated-dose toxicity studies (including carcinogenicity and reproduction toxicity) on propane alone.

Propane (purity: >99.9%) did not induce mutations when tested with and without an induced rat liver metabolic activation system in *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 at concentrations of 5-50% (v/v) in a desiccator (exposure time: 6 hours) (Kir80).

**Butane**

Injection of liquid butane into the anterior eye chamber of rabbits did not cause disturbance, and all effects disappeared in 2-4 days (Gra74).

Kane and Alarie exposed groups of male Swiss-Webster mice to photochemical oxidant mixtures generated by a reaction between various hydrocarbons, among which butane, and nitrogen dioxide in the presence of ultraviolet light. Meanwhile, the respiratory rates of the mice were monitored. The initial hydrocarbon concentrations ranged from 0.4 to 18 ppm (0.9-42.7 mg/m$^3$) with the initial nitrogen dioxide concentration being one-third of the initial hydrocarbon concentration. Concomitant exposure to butane and nitrogen dioxide did not significantly affect respiratory rate, indicating no irritation of the upper respiratory tract. The authors also reported that butane did not cause irritation to the eyes of the mice (Kan78). In guinea pigs, exposure to concentrations of butane of 21,000-56,000 ppm (ca. 50,800-135,000 mg/m$^3$) caused increased respiratory rate, sniffing, and chewing movements, animals recovering quickly after cessation of exposure (Low87b).

Acute LC$_{50}$ values were 658,000 and 680,000 mg/m$^3$ (ca. 270,000 and 279,000 ppm) in rats (exposure duration: 4 hours) and mice (2 hours), respectively (Shu69). In mice, 40 and 60% of the animals died at 2-hour exposures to ca. 653,000 and 750,000 mg/m$^3$ (270,000 and 310,000 ppm), respectively.
respectively. Slight anaesthesia was observed at exposure to 130,000 or 220,000 ppm (314,600 and 532,400 mg/m³) for 25 and 1 minute, respectively, while 15-minute exposure to the higher concentration induced complete anaesthesia (Ber95b, Low87b). In dogs, concentrations of 200,000-250,000 ppm (484,000-605,000 mg/m³) caused anaesthesia and mortality within a few minutes. Other studies showed butane to sensitize the heart to epinephrine-induced cardiac arrhythmias or ventricular fibrillation at levels of 150,000-900,000 (363,000-2,178,000 mg/m³), for 10 minutes, and of 10,000-200,000 ppm (24,200-484,000 mg/m³), for 2 minutes to 2 hours, respectively (Ber95b, Low87b), while exposure to 5000 ppm (12,100 mg/m³) had caused haemodynamic changes in anaesthetized dogs, such as a decrease in cardiac output, left ventricular pressure, and stroke volume, a decrease in myocardial contractility, and aortic pressure (Low87b).

Halder et al. examined the toxicity of a hydrocarbon blend vapour consisting of 25% (w/w) each of butane, pentane, isobutane, and isopentane by exposing rats (Sprague-Dawley; n=10/sex/group) to, analytical, time-weighted average, total hydrocarbon concentrations of 0, 116, 1150, or 11,800 mg/m³ (0, 44, 432, and 4437 ppm). Particular attention was paid to effects on the kidneys. Histological examinations were also done on the brain, heart, liver, spleen, adrenals, and gonads. During exposure, no clinical signs of toxicity were observed. Post-mortem examinations did not show macroscopic or microscopic changes in any of the organs examined in any of the treated groups and no evidence of the presence of the male-rat-specific, hydrocarbon-induced nephropathy (Hal86). From this study, the committee concluded that the NOAEL for rats is at least 11,800 mg/m³ for total hydrocarbons and at least 2950 mg/m³ (1210 ppm) for butane.

The same research group exposed 20 male and 10 female rats (Fischer 344) to analytical, time-weighted average, concentrations of a mixture of butane and pentane of 1017 and 4489 ppm, for 13 weeks. The relative proportions of butane in the mixture were 51.5 and 47.5 wt%, respectively. A control group consisting of 40 male and 20 female animals was included. At day 28, necropsies were performed for half of the male rats of each treatment group. All animals survived exposure. Aranyi et al. reported possible treatment-related, but not dose-related, signs of toxicity including transient hunched posture and/or lethargy and intermittent tremor and statistically significantly decreased body weights for both males and females by test week 3 and 4. At the end of the study, body weights were comparable to those of controls. At post-mortem examinations, liver and kidney weights were not affected and no gross, treatment-related lesions were observed. Only the kidneys were examined microscopically and
scored based on the presence of hyaline droplet accumulation in the proximal tubule epithelial cells, of foci of regenerative tubular epithelium in the cortical region of the kidney, and of dilated tubuli filled with granular material located at the junction between the inner and outer stripes of the medulla. These kidney lesions were seen in all male treated and control groups but not in the female groups. Compared with controls, there were dose-related, not statistically significant increases in scores at the 28-day interim kill, but scores did not differ between male groups at study termination (Ara86). From this study, the committee concluded that the NOAEL for rats is at least 4489 ppm for the butane/pentane mixture and at least 2343 ppm (5670 mg/m³; calculated based on relative proportion of butane in this mixture of 47.5 wt%) for butane.

The committee did not find data from repeated-dose toxicity studies (including carcinogenicity and reproduction toxicity) on butane alone.

Tested under similar conditions as propane (see above), butane (purity: 99.7%) was negative in *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 (Kir80). Shimizu et al. obtained negative results as well when butane (purity: 99%) was tested with and without metabolic activation in these 5 *Salmonella* strains as well as in *E. coli* strain WP2 *uvrA* at concentrations of 250-10,000 ppm (Shi85).

Butane was negative in the sex-linked recessive lethal mutation assay in *D. melanogaster*, exposed by inhalation to 350,000 ppm n-butane (Fou94).

7 Existing guidelines

The current administrative occupational exposure limits (MAC) for LPG and butane in the Netherlands are 1800 and 1430 mg/m³ (1000 and 600 ppm), 8-hour TWA, respectively. For propane, no administrative MAC value has been established. Propane is considered to act as a simple asphyxiant, when present at high concentrations in air, by reducing the oxygen content air by dilution to such an extent that life cannot be supported. In order to prevent this, the content of oxygen in air should be at least 18% (v/v).

Existing occupational exposure limits for LPG, propane, and butane in some European countries and in the USA are summarised in the annex.
8 Assessment of health hazard

Propane
Data from studies using mouse liver microsomal suspensions and mice suggest that propane might be metabolised into 2-propanol and acetone through oxidation by the microsomal enzyme system and alcohol dehydrogenase, respectively. Propane has been detected in blood, brain, liver, and kidneys of mice and men and in the lungs of men.

Human data include several cases of fatal (intentional) inhalation of propane. In one case of long-term propane abuse, euphoria, ataxia, light-headedness, severe headache, and memory loss were reported, but no abnormalities were found at physical examination (including a neurological assessment, and laboratory - blood, liver function – tests). No changes in EEGs, adrenocortical functions, pulmonary functions, neurological response, subjective response, cardiac function, cognitive response, or visual evoked response were seen in volunteers exposed to 1000 ppm (1840 mg/m³) propane, 8 hours/day, for 9 days. Ten-minute exposures to 10,000 ppm (18,400 mg/m³) did not produce symptoms, but 2-minute exposures up to 100,000 ppm (184,000 mg/m³) resulted in distinct vertigo, but no mucosal irritation of nose, eyes, or respiratory tract. Dermal contact with liquid propane can cause frostbite.

In guinea pigs exposed to ca. 44,000-53,000 (24,000-29,000 ppm) or 86,000-101,000 mg/m³ (47,000-55,000 ppm) for 5-120 minutes, irregular breathing, nausea, retching, stupefaction, tremors (at 86,000-101,000 mg/m³), and narcosis (at levels of ca. 92,000 mg/m³ or 50,000 ppm), but no mortality or pathological changes were observed. Five-minute exposure by tracheal cannula to concentrations of 360,000 mg/m³ (200,000 ppm) did not induce bronchoconstriction, respiratory depression, arrhythmia, or myocardial depression in rhesus monkeys. In mice and dogs, 6-10 minute exposure to 180,000 mg/m³ (100,000 ppm) did not induced arrhythmia but (weakly) sensitised the heart to epinephrine-induced cardiac arrhythmias.

The committee did not find data from experiments on the toxicity (including carcinogenicity and reproduction toxicity) of propane following repeated exposure.

Apart from a negative result in an in vitro mutation assay in S. typhimurium, the committee did not find data from mutagenicity and genotoxicity studies on propane.
The committee considers the toxicological database on propane too poor to justify recommendation of a health-based occupational exposure limit.

**Butane**

In humans, absorption of butane was stated to be 30-45% of the dose inhaled. From experiments in which rats were exposed to butane concentrations of 100 ppm (240 mg/m³) for 80 minutes, the committee calculated absorption to be ca. 10%. Although the committee did not find data on absorption through the skin, dermal penetration of butane is expected to be low since skin contact is transient due to the volatility of the compound. Following exposure of rats to lethal concentrations of ca. 650,000 mg/m³ (ca. 270,000 ppm), for 4 hours, the highest concentrations of butane were found in the perirenal fat tissue, followed by the brain, spleen, liver, and kidney. *In vivo* and *in vitro* experiments suggest that butane might be metabolised into 2-butanol by the microsomal enzyme system followed by conjugation with glucuronic acid or oxidation into 2-butanol by alcohol dehydrogenase.

Human data on effects of exposure to butane mostly concern its abuse as an inhalant, from, e.g., lighters or hair/deodorant sprays. Butane abuse was frequently fatal, mostly due to heart failure (arrhythmias, ventricular fibrillation, asystole). In non-fatal cases, butane induced severe acute neurological (seizure, somnolence, coma) or cardiovascular (ventricular fibrillation, asystole, collapse) complications and minor symptoms such as nausea, dizziness, vomiting, headache, and sore throat. However, no quantitative exposure data were available.

Butane was not irritating to the eyes of rabbits when injected as a liquid into the anterior chamber or to the upper respiratory tract of mice. In guinea pigs, some transient irritation (increased respiratory rate, sniffing, and chewing movements) during exposure to concentrations of 21,000-56,000 ppm (ca. 50,800-135,000 mg/m³) was observed. Acute LC₅₀ values were 658,000 and 680,000 mg/m³ (269,780 and 278,800 ppm) in rats (exposure duration: 4 hours) and mice (2 hours), respectively. In mice, 25-minute to 130,000 ppm (314,600 mg/m³) or 1-minute exposure to 220,000 ppm (532,400 mg/m³) induced slight anaesthesia; 15-minute exposure to 222,000 ppm complete anaesthesia. In dogs, concentrations of 200,000-250,000 ppm (484,000-605,000 mg/m³) caused anaesthesia and mortality within a few minutes. Butane had a cardiac sensitising effect in dogs.

The committee did not find data from experiments on the toxicity (including carcinogenicity and reproduction toxicity) of butane following repeated exposure.
Data on rats exposed to mixtures of aliphatic hydrocarbons showed that exposure to a mixture containing an estimated concentration of butane of 2950 mg/m³ did not induce an increase in the incidence of macroscopic or microscopic organ lesions. Exposure to another mixture containing an estimated concentration of butane of 5670 mg/m³ increased the incidence of kidney lesions (hydrocarbon-induced nephropathy) when compared to controls. However, in these studies, effect levels were not identified and effects on the central nervous system, a potential target organ, were not addressed. Therefore, the committee is of the opinion that the studies cannot be used as starting points in deriving a health-based occupational exposure limit.

Butane was negative in in vitro mutation assays in *S. typhimurium* and *E. coli* and in a sex-linked recessive lethal mutation assay in *D. melanogaster*.

The committee considers the toxicological database on butane too poor to justify recommendation of a health-based occupational exposure limit.

Based on the animal data from studies with butane-containing mixtures (Ara86, Hal86), the committee concludes that there is no reason to suspect that the current occupational exposure limit of 1430 mg/m³ (600 ppm), as an 8-hour time-weighted average, is too high.

**LPG**

Apart from a few fatal cases and one case of nausea, malaise, general weakness of the lower limbs, and acute hepatitis, the committee did not find any information from reports on toxic effects of LPG in men and experimental animals.

The committee considers the toxicological database on LPG too poor to justify recommendation of a health-based occupational exposure limit.

Based on the available human and animal data on butane, the committee has no reason to suspect that the current administrative MAC value for LPG of 1800 mg/m³ (1000 ppm), as an 8-hour time-weighted average, is too high.

**References**

Liquefied petroleum gas (LPG), Propane, Butane


ACG04b American Conference of Governmental Industrial Hygienists (ACGIH). 2004 TLVs® and BEIs® based on the documentation of the Threshold Limit Values for chemical substances and physical agents & Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, 2004: 15, 36, 47.


Arb02 Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2002: 18, 26, 35 (At-vejledning C.0.1).

Avis74 Aviado DM, Belej MA. Toxicity of aerosol propellants in the respiratory and circulatory systems. I. Cardiac arrhythmia in the mouse. Toxicology 1974; 2: 31-42.


Bel74 Belej MA, Smith DG, Aviado DM. Toxicity of aerosol propellants in the respiratory and circulatory systems. IV. Cardiotoxicity in the monkey. Toxicology 1974; 2: 381-95.


Cha02 Chaudhry S. Deaths from volatile substance misuse fall. BMJ 2002; 325: 122.
Health-based Reassessment of Administrative Occupational Exposure Limits

134-18


Gra74 Grant WM. Toxicology of the eye. 2nd ed. Springfield IL, USA: Charles C Thomas, 1974.


Kat98 Kattenwinkel HD. Product Manager Fuels. Shell, the Netherlands. Letter dated 011598.


Liquefied petroleum gas (LPG), Propane, Butane
Rut86  Ruth JH. Odor thresholds and irritation levels of several chemical substances: a review. Am Ind Hyg Assoc J 1986; A-142-51.


## Annex

Occupational exposure limits for liquefied petroleum gas (LPG) in various countries.

<table>
<thead>
<tr>
<th>country</th>
<th>organisation</th>
<th>occupational exposure limit</th>
<th>time-weighted average</th>
<th>type of exposure limit</th>
<th>note(^a)</th>
<th>reference(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>the Netherlands</td>
<td>- Ministry of Social Affairs and Employment</td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td>administrative</td>
<td>SZW04</td>
</tr>
<tr>
<td>Germany</td>
<td>- AGS</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>TRG04</td>
</tr>
<tr>
<td></td>
<td>- DFG MAK-Kommission</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>DFG04</td>
</tr>
<tr>
<td>Great Britain</td>
<td>- HSE</td>
<td>1000</td>
<td>1750</td>
<td>8 h</td>
<td>OES</td>
<td>HSE03</td>
</tr>
<tr>
<td></td>
<td>1250</td>
<td>2180</td>
<td>15 min</td>
<td>STEL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Swe90</td>
</tr>
<tr>
<td>Denmark</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Arb02</td>
</tr>
<tr>
<td>USA</td>
<td>- ACGIH</td>
<td>1000(^d)</td>
<td>-</td>
<td>8 h</td>
<td>TLV</td>
<td>ACG04b</td>
</tr>
<tr>
<td></td>
<td>- OSHA</td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td>PEL</td>
<td>ACG04a</td>
</tr>
<tr>
<td></td>
<td>- NIOSH</td>
<td>1000</td>
<td>1800</td>
<td>10 h</td>
<td>REL</td>
<td>ACG04a</td>
</tr>
<tr>
<td>European Union</td>
<td>- SCOEL</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>EC04</td>
</tr>
</tbody>
</table>

\(^a\) S = skin notation; which means that skin absorption may contribute considerably to the body burden; sens = substance can cause sensitisation.

\(^b\) Reference to the most recent official publication of occupational exposure limits.

\(^c\) Reference to propane: 1000 ppm/1800 mg/m³, 8-hour TWA.

\(^d\) Reference to ‘aliphatic hydrocarbon gases: alkane [C\(_1\)-C\(_4\)]’. 

---

134-21 Liquefied petroleum gas (LPG), Propane, Butane
Occupational exposure limits for propane in various countries.

<table>
<thead>
<tr>
<th>country</th>
<th>organisation</th>
<th>occupational exposure limit</th>
<th>time-weighted average</th>
<th>type of exposure limit</th>
<th>note</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>the Netherlands</td>
<td>Ministry of Social Affairs and Employment</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>SZW04</td>
</tr>
<tr>
<td>Germany</td>
<td>AGS</td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td></td>
<td>TRG04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4000</td>
<td>7200</td>
<td>15 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DFG MAK-Kommission</td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td></td>
<td>DFG04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2000</td>
<td>3960</td>
<td>15 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Great-Britain</td>
<td>HSE</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>HSE02</td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>Swe00</td>
</tr>
<tr>
<td>Denmark</td>
<td></td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td></td>
<td>Arb02</td>
</tr>
<tr>
<td>USA</td>
<td>ACGIH</td>
<td>1000f</td>
<td>-</td>
<td>8 h</td>
<td></td>
<td>ACG04b</td>
</tr>
<tr>
<td></td>
<td>OSHA</td>
<td>1000</td>
<td>1800</td>
<td>8 h</td>
<td>PEL</td>
<td>ACG04a</td>
</tr>
<tr>
<td></td>
<td>NIOSH</td>
<td>1000</td>
<td>1800</td>
<td>10 h</td>
<td>REL</td>
<td>ACG04a</td>
</tr>
<tr>
<td>European Union</td>
<td>SCOEL</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td>EC04</td>
</tr>
</tbody>
</table>

- S = skin notation; which means that skin absorption may contribute considerably to the body burden; sens = substance can cause sensitisation.
- Reference to the most recent official publication of occupational exposure limits.
- Asphyxiant.
- Maximum number per shift: 4, with a minimum interval between peaks of 1 hour.
- Listed among substances with MAK values but no pregnancy risk group classification.
- Reference to `aliphatic hydrocarbon gases: alkane (C1-C4)`.

134-22  Health-based Reassessment of Administrative Occupational Exposure Limits
### Occupational exposure limits for butane in various countries.

<table>
<thead>
<tr>
<th>Country</th>
<th>Organisation</th>
<th>Occupational exposure limit</th>
<th>Time-weighted average</th>
<th>Type of exposure</th>
<th>Note</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>the Netherlands</td>
<td>Ministry of Social Affairs and Employment</td>
<td>600</td>
<td>1430</td>
<td>8 h</td>
<td></td>
<td>SZW04</td>
</tr>
<tr>
<td>Germany</td>
<td>AGS</td>
<td>1000</td>
<td>2350</td>
<td>8 h</td>
<td></td>
<td>TRG04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4000</td>
<td>9400</td>
<td>15 min</td>
<td></td>
<td>DFG04</td>
</tr>
<tr>
<td></td>
<td>DFG MAK-Kommission</td>
<td>1000</td>
<td>2400</td>
<td>8 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4000</td>
<td>9600</td>
<td>15 min</td>
<td>a</td>
<td></td>
</tr>
<tr>
<td>Great-Britain</td>
<td>HSE</td>
<td>600</td>
<td>1450</td>
<td>8 h</td>
<td>OES</td>
<td>HSE02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>750</td>
<td>1810</td>
<td>15 min</td>
<td>STEL</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>Swe00</td>
</tr>
<tr>
<td>Denmark</td>
<td></td>
<td>500</td>
<td>1200</td>
<td>8 h</td>
<td></td>
<td>Arb02</td>
</tr>
<tr>
<td>USA</td>
<td>ACGIH</td>
<td>1000</td>
<td>-</td>
<td>8 h</td>
<td>TLV</td>
<td>ACG04b</td>
</tr>
<tr>
<td></td>
<td>OSHA</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>ACG04a</td>
</tr>
<tr>
<td></td>
<td>NIOSH</td>
<td>800</td>
<td>1900</td>
<td>10 h</td>
<td>REL</td>
<td>ACG04a</td>
</tr>
<tr>
<td>European Union</td>
<td>SCOEL</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>EC04</td>
</tr>
</tbody>
</table>

* S = skin notation; which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

b Reference to the most recent official publication of occupational exposure limits.

c Maximum number per shift: 4, with a minimum interval between peaks of 1 hour.

d Listed among substances with MAK values but no pregnancy risk group classification.

e Reference to: ‘aliphatic hydrocarbon gases: alkane (C₁–C₄)’.