Interviews with friends and school officials revealed that sniffing of butane lighter fuel is a common practice among many children at upper middle class schools in Cincinnati. The second subject was avowedly antidrugs and did not consider sniffing to be "drug abuse." Ironically, his mother had discussed the first fatality with him. His response was that the dead teenager was "probably doing it wrong," again attesting to the unfortunate, uneducated familiarity with this form of abuse. Many empty butane canisters were subsequently found in this teenager's bedroom.

There are few reports of nonfatal incidents with "butane abuse". Inhalation of butane lighter fluid by a 15-year-old boy, reported in the British literature, resulted in severe anterior chest pain, agitation, and collapse. In the emergency department, ventricular fibrillation occurred; this condition reverted to sinus rhythm after cardioversion and lidocaine treatment (Gunn et al. 1989).

There is also some reported experience with "fire breathing" or "torch breathing" after butane inhalation. Cartwright reported a 19-year-old fire breather who inhaled butane gas from a cigarette lighter and then ignited it after forcible exhalation (Cartwright et al. 1983). The subject suffered dyspnea, fever, malaise, and hypoxia and had extensive pulmonary infiltrates. Marsh (1984) reported the case of a 14-year-old boy who developed hemorrhagic esophagitis and gastritis after repeated fire breathing.

A recent report details a 17-year-old adolescent's propane abuse practices (Wheeler et al. 1992). The authors speculate that the practice may be widespread.

Several sudden sniffing deaths due to propane and butane have been presented. Since the abandonment of fluorocarbons, replacement fuels and propellants (such as butane and propane) probably represent the most common sudden sniffing death hazard. Health care providers need to be aware that the profile of the teenager who inhales volatiles does not include only the ethnic lower socioeconomic classes. Reported investigations and many other communications lead us to believe that abuse of these readily available inhalants has reached epidemic proportions, indicating an urgent need for preventive efforts directed at teenagers and their parents with emphasis on the risk of sudden sniffing death.

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ALIPHATIC HYDROCARBON GASES: ALKANES [C_1–C_4]

Molecular formulas: CH_4; C_2H_6; C_3H_8; C_4H_{10}

METHANE

CAS number: 74-82-8

Synonyms: Biogas; Fire damp; Marsh gas; Methyl hydride; Methane, various grades; Natural gas; R 50 (refrigerant)

Molecular formula: CH_4

ETHANE

CAS number: 74-80-0

Synonyms: Dimethyl; Ethane; ethane, C.P. grade, 99%; Ethyl hydride; Methylmethane

Molecular formula: C_2H_6

PROPANE

CAS number: 74-98-6

Synonyms: Dimethyl methane; n-Propane; Propane, various grades

Molecular formula: C_3H_8

BUTANE

CAS number: 106-97-8

Synonyms: n-Butane; Methylethyl Methane; Butane; n-butane, various grades

Molecular formula: C_4H_{10}

ISOBUTANE

CAS number: 75-28-5

Synonyms: Methylpropane; 2-methylpropane; Isobutane; isobutane, various grades

Molecular formula: C_4H_{10}

PETROLEUM GAS; LIQUEFIED PETROLEUM GAS, LPG

CAS number: 68476-85-7

Synonyms: LPG; Petroleum gases, liquefied

NATURAL GAS

CAS number: 8006-14-2

Synonym: LNG

TLV–TWA, 1000 ppm

Summary

A TLV–TWA of 1000 ppm is recommended for all C_1 to C_4 alkane hydrocarbon gases. This limit applies to individual gases (methane, ethane, propane, butane, isobutane) and mixtures of these gases, to include liquefied petroleum gas and natural gas. This is a complete list of gases to which this TLV applies. The TLV is believed to be protective against potential health effects that include central nervous system (CNS) depression and cardiac sensitization. The TLV is based upon the abilities of these gases to produce weak depressant effects on the CNS at high concentration levels approaching the lower flammability limit. It has also been reported that ethane and propane can induce cardiac arrhythmias under certain conditions leading to ventricular fibrillation that can result in death in the presence of high epinephrine levels. Sufficient data were not available to recommend sensitization (SEN) or carcinogenicity notations or a TLV–STEL.

Physical and Chemical Properties

Selected physical and chemical properties are presented in Table 1.[1–5] Methane, ethane, and propane are flammable gases that occur in natural gas at concentrations of 60% to 80%, 5% to 9%, and 3% to 18%, respectively.

Liquefied petroleum gas (LPG) is highly flammable and is a dangerous fire and explosion hazard with a boiling range between –44° and +1°C.[4] An odor threshold ranging from 5,000 to 20,000 ppm has been reported.[1] A foul-smelling odorant (e.g., ethyl mercaptan) is added commercially. The principal components of LPG are propane, n-butane, and isobutane; however, it may contain ethane, n-pentane, and small quantities of, olefin gases (e.g., propylene, 1-butene, cis-2-butene, trans-2-butene, 1,3-butadiene) as well. In general the specifications for LPG limits for physical properties; consequently, the composition of the commercial grade product varies between wide limits. LPG that is recovered

TABLE 1. Relevant Physical and Chemical Properties[1–5]

Parameters	Methane	Ethane	Propane	n-Butane	Isobutane
CAS RN	74-82-8	74-84-0	74-98-6	106-97-8	75-28-5
Molecular formula	CH_4	C_2H_6	C_3H_8	C_4H_{10}	C_4H_{10}
Appearance	Odorless, colorless gas	Odorless, colorless gas	Odorless, colorless gas	Slight odor, colorless gas	Slight odor, colorless gas
Molecular weight	16.042	30.069	44.096	58.123	58.123
Boiling point (°C)	–161.49	–88.63	–42.07	–0.50	–11.73
Flash point (°C)	–187.78	–135.0	–183.27	–60.0	–82.78
Lower flammability limit	5% (50.000 ppm)	3% (30,000 ppm)	2.1% (21,000 ppm)	1.8% (18,600 ppm)	1.8% (18,000 ppm)
Specific gravity (25°C)	0.422	0.374	0.5077	0.5844	0.5631
Vapor pressure (760 torr; 25°C)	Gas	Gas	Gas	Gas	Gas
Vapor density at 25°C (air = 1)	0.55	1.04	1.56	2.07	2.07
Water solubility	Very slight	Insoluble	Slight	Slight	Slight
Odor threshold	303 mg/m^3	185–1106 mg/m^3	1800–36,000 mg/m^3	2.9–14.6 mg/m^3	45 mg/m^3
Conversion factors at 25°C and 760 torr	1 ppm = 0.66 mg/m^3 1 mg/m^3 = 1.515 ppm	1 ppm = 1.23 mg/m^3 1 mg/m^3 = 0.813 ppm	1 ppm = 1.80 mg/m^3 1 mg/m^3 = 0.555 ppm	1 ppm = 2.38 mg/m^3 1 mg/m^3 = 0.42 ppm	1 ppm = 2.38 mg/m^3 1 mg/m^3 = 0.42 ppm

TABLE 2. Pharmacologic Effects[A]

Effect	Methane (ppm)	Ethane (ppm)	Propane (ppm)	n-Butane (ppm)	Isobutane (ppm)
CNS depression (narcosis)[B]	300,000	130,000	47,000	17,000	24,000
Cardiac arrhythmia in presence of epinephrine		150,000 to 190,000	100,000	—	50,000 to 100,000
Anesthesia	870,000 cats		630,000 cats 550,000 guinea pigs	130,000 to 450,000	
LC_{50}	900,000 cats		>550,000 guinea pigs (4-hr)	280,000 rats (4-hr)	124,000 mice (1-hr)

[A]Compiled from Avaido,[8] Cavender,[4] Clark & Tinston,[9] Krantz,[10] Low,[11] Reinhardt.[12] Shugaev,[13] and von Oettinger.[14]
[B]Predicted using the 1993 Drummond model.[15]

from natural gas processing is essentially free of unsaturated hydrocarbons (e.g., olefins such as propylene and butadiene). LPG is available commercially as propane (often found in colder climates), butane (more widely found in the Southern states due to its higher boiling and freezing points), and butane-propane mixtures.[2,3]

Natural gas is colorless, odorless, and flammable. It occurs naturally along with petroleum deposits in marshes or from waste decomposition. Methane is its predominant component, mixed with ethane, propane, and butane.

History

Previously, separate TLVs were developed for some of these gases. A TLV–TWA of 1000 ppm for LPG was adopted in 1966. The individual C_1 to C_4 aliphatic hydrocarbons were identified as "simple asphyxiants, without other significant physiologic effects."[6] A TLV–TWA of 800 ppm was adopted for butane in 1981, and a TLV–TWA of 2500 ppm for propane was adopted in 1998, each based on the desire to maintain airborne concentrations below 10% of the lower flammability limit, plus weak pharmacological activity at high exposures in the case of propane. For the other asphyxiant gases, the recommendation was only to keep oxygen levels above 18% by volume (at one atmosphere of pressure). This recommendation was changed to 19.5% in 2004. This suggests that an unprotected person may enter an atmosphere containing up to 14% by volume of hydrocarbon gases, since approximately 14% of an inert material will dilute the oxygen content of air from 21% to 18%. At 14% by volume of hydrocarbon gas, there will be significant physiologic effects as well as flammability hazard.

Major Sources of Occupational Exposure

Hydrocarbon gases are common in some areas of both upstream and downstream petroleum operations. The precise composition varies depending on the source of the gas but typically contains methane, ethane, propane, and other light hydrocarbons. Hydrocarbon gases are used as domestic, industrial, automotive, welding, brazing, and metal cutting fuels. They are used to purge refinery units and to operate pneumatic equipment. The gases may also be found in tanks, wells, and as fugitive emissions from leaky pumps, meters, and valves used in petroleum service.

Methane

Methane is an end product of anaerobic decay. As such, it is the major constituent of natural gas, where it occurs at concentrations between 600,000 and 800,000 ppm.[4] Methane is also found in coal deposits and, when present during mining operations, can form explosive mixtures known as fire damp.[7] Methane is also commonly produced by the decomposition of organic matter by a variety of bacterial processes (particularly in municipal landfills where concentrations can exceed 250,000 ppm), and the gas is used as a fuel in sewage plants. A common name for methane is marsh gas. Methane is used in the production of acetylene, ammonia, methanol, hydrogen cyanide, and halogenated products such as methyl chloride.[7] Methane is usually accompanied by other volatile low-molecular-weight hydrocarbons and sulfur compounds.[7]

Natural Gas and LPG

LPG is produced from natural gas and is recovered during petroleum refining. Its main uses are as fuels and feedstocks for the production of a wide variety of chemicals. Residential and commercial demands represent nearly half of all LPG sales. The second largest use is in the manufacture of petroleum and polymer intermediates.[2]

Animal Studies

A comparison of the pharmacologic effects of some related low-molecular-weight hydrocarbons in animals is presented in Table 2. Hypoxia, as well as the stress that may occur with high concentrations of these gases, can elevate epinephrine. Thus, the asphyxiant, CNS, and cardiac arrhythmia effects may act synergistically. As mixtures, the effects of

these hydrocarbon gases are cumulative. The estimated concentrations at which these various effects occur vary somewhat among the gases. See below for further discussion.

Acute

From a toxicologic standpoint, methane and ethane are of low anesthetic potency and are practically inert; however, at very high concentrations, they act as a simple asphyxiant and can cause suffocation by displacement of oxygen from breathing atmosphere,[2,4,11,16,17] below the critical level of 16% oxygen that is required to sustain life.[18] There is only a very slight margin between the anesthetic concentration of methane and that causing death; a concentration of at least 87% (870,000 ppm) was required to anesthetize cats, but exposure at 90% (900,000 ppm) was lethal.[14] A concentration of 87% caused asphyxiation, and respiratory arrest occurred in mice at concentrations on the order of 90%.[19] Laboratory animals exposed at 2.5% to 5.5% (25,000–55,000 ppm) ethane developed irregular respiration after 2 hours of exposure.[11,20]

The LC_{50} for propane was greater than 800,000 ppm (80%) when groups of six male and six female rats were exposed for 15 minutes to various concentrations of propane in air.[9] The effective concentration (EC_{50}) causing CNS depression in half of the tested rats was 280,000 ppm (28%) propane administered for 10 minutes.[9] Where deaths occurred, it was during, not after, exposure and was associated with depressant effects on the CNS. Recovery from nonlethal exposure was rapid, and affected animals appeared normal within 10 minutes. Propane caused early respiratory depression in the monkey.[8] The depression of breathing was the only toxic endpoint in monkeys when exposed at 100,000 to 200,000 ppm (10%–20%) propane for 15 minutes. Guinea pigs exposed to propane concentrations between 24,000 and 29,000 ppm (24%–29%)or 47,000 and 55,000 ppm (47%–55%) for 5 to 120 minutes developed irregular breathing at lower concentrations and tremors at the highest concentrations. The effects were reversible upon cessation of exposure, and there were no pathological organ changes in these animals at necropsy.[11] Blood pressure changes were reported in dogs after exposure at 25,000 ppm (2.5%) propane. Effects on blood pressure, heart stroke rate/volume, and pulmonary vascular resistance were also reported after exposures at 33,000 ppm (3.3%).[21]

The 4-hour LC_{50} for n-butane in rats was 658 mg/L or about 280,000 ppm (28%).[13] n-Butane is anesthetic to mice at 130,000 ppm (13%) in 25 minutes and at 220,000 (22%) in 1 minute, whereas 25% was required for anesthesia in the dog.[4] n-Butane is reported to be a weak cardiac sensitizer in the dog, and 5000 ppm in the anesthetized dog may cause hemodynamic changes.[4]

The 1-hour LC_{50} for isobutane for the mouse was 52 mg/L or about 22,000 ppm (22%).[4] Mice exposed near the LC_{50} exhibited CNS depression, rapid and shallow respiration, and apnea. Isobutane may also be a cardiac sensitizer.[4] In the anesthetized dog, there were no significant effects up to 2% isobutane, but there were significant hemodynamic changes from 2.5% through 10%; in the dog anesthesia occurs at 45% after 10 minutes of exposure.[4]

Cardiac arrhythmia was studied in dogs following inhalation of ethane and propane at high concentrations. Although the criteria used for cardiac arrhythmia may have differed between studies, all exposures resulted in responses indicative of cardiac arrhythmia. In one study, cardiac arrhythmia, observed as multifocal ventricular tachycardia, occurred in dogs exposed to ethane (2 of 4 dogs) and propane (3 of 3 dogs). The specific exposure was not defined for the hydrocarbon gases studied; however, a range of 150,000 to 900,000 ppm for gaseous compounds was cited. Ventricular fibrillation and death occurred in some animals.[10] In another study, dogs exposed to propane at 100,000 and 200,000 ppm for 5 minutes produced cardiac arrhythmias or multiple ventricular beats 17% and 58% of the time, respectively. Cardiac arrhythmia did not occur in dogs at 5000 ppm propane.[12] Additionally, a 5-minute exposure to 18% propane (by volume) with concurrent epinephrine administration induced cardiac arrhythmia in 50% of exposed dogs (i.e., the EC_{50}).[22] A similar effect occurred in mice at 10% concentration.[8]

LPG has a low potential for acute effects. Depressant effects on the CNS were observed at 280,000 ppm in 50% of the exposed rats and recovery was rapid, within 10 minutes.[9]

Subchronic

Monkeys were exposed at 750 ppm propane via inhalation for 90 days. No abnormalities were noted.[11]

Chronic/Carcinogenicity

No data were available on effects from chronic exposure to the C_1–C_4 alkane hydrocarbon gases.

Genotoxicity

Propane gas showed no mutagenic activity when tested in the Ames assay at concentrations up to 500,000 ppm (50% volume).[22]

Reproductive/Developmental Toxicity

No data were available on reproductive effects from chronic exposure to the C_1–C_4 alkane hydrocarbon gases.

Absorption, Distribution, Metabolism, and Excretion

Methane was readily absorbed and metabolized

by mammals; however, uptake in humans was less rapid than in the rat. Following absorption, methane was metabolized to only a very limited extent.[16] When inhaled, the majority of the absorbed dose was exhaled unchanged. Propane was metabolized by various microorganisms such as *Microbacterium vaccae* via the succinate pathway.[23] There were no pharmacokinetic data available for methane, ethane, and propane.

Human Studies

Methane is neither irritating to the skin, eyes, nose, throat, and lungs nor is it considered poisonous. The major hazards associated with methane handling, transport, and control were due to its and flammability and explosive nature.[4] Liquefied petroleum gas may cause frostbite on skin contact.[4]

Methane, ethane, and propane have practically no physiological effects under normal conditions of exposure.[4] Medical surveillance revealed no untoward subjective symptoms or objective signs of illness in eight adult volunteers exposed to a mixture of propane and isobutane in a chamber at concentrations as high as 1030 ppm propane and 143 ppm isobutane for 1, 2, or 8 hours. Objective measurements included electrocardiogram (no arrhythmia was observed), adrenocorticotropic hormone (normal), lung function, neurological tests (modified Romberg and heel-to-toe test), electroencephalogram, cognitive tests, and visual evoked response. Two subjects showed considerable variations in the visual evoked response, but exposure-related effects were not detected.[24]

A 10-minute exposure at 10,000 ppm butane resulted in drowsiness, but no other evidence of systemic effects were present.[4] Stewart et al.[24] found no untoward subjective or abnormal physiological responses in human subjects exposed to isobutane for single 8-hour periods at 1000 ppm or for 8 hours/day, 5 days/week for 2 weeks at 500 ppm. However, during the second week of exposure at 500 ppm, a reduction in the visual evoked response wave amplitude was observed. The significance of this finding was considered uncertain.

Mathew et al.[25] reported that a 16-year-old girl had inhaled an estimated 20 liters of butane in 1 year. Initial abuse produced visual hallucinations. Continual abuse was associated with irregular school attendance; deterioration in social functioning, leading to isolation; increasing irritability and impulsivity; and was easily provoked. The commercial butane contained varying proportions of propane, butane, and isobutane.

CNS Effects

The onset of CNS effects (narcosis) from inhalation exposures to light hydrocarbon gases in the workplace can be predicted using a model designed to calculate the potency of anesthetic gases.[15] Narcosis was part of a continuum of CNS effects which included surgical anesthesia. The model was based on lipid solubility (air:olive oil partition coefficients) since anesthetic gases were believed to exert their action by dissolving in the lipid bilayer that form cell membranes. The model also predicted the speed of action of gases. Typically, the less soluble in blood, the faster the action of the gas. Gases that are insoluble in the blood will rise quickly toward equilibrium with the inhaled mixture. The model has been validated using human experience from underwater diving (nitrogen narcosis) and workplace exposure to toluene.

Methane was predicted to induce CNS effects (narcosis) at 300,000 ppm, based on its air:olive oil partition coefficient of 0.89. Because methane displaces oxygen (to 18%) in air at 14% or 140,000 ppm before CNS effects become apparent, methane was considered to be a simple asphyxiant.[15] Ethane is predicted to induce narcosis at 130,000 ppm, based on its air:olive oil partition coefficients of 2.1. Likewise, propane, butane, and isobutane were predicted to induce narcosis at 47,000, 17,000, and 24,000 ppm, respectively, based on air:olive oil partition coefficients of 5.9 (propane), 17 (butane), and 12 (isobutane). This model predicted that ethane, propane, butane, and isobutane were not just simple asphyxiants, but fast-acting agents which induced narcosis (loss of judgment, disorientation, dizziness, light headedness) below the concentration for asphyxiation (140,000 ppm, 14%). Table 2 presents data relevant to predicting acute narcosis. Further, these results indicated CNS effects were expected to occur in less than 15 minutes following inhalation exposures to propane, based on the predicted blood:air partition coefficients of less than 0.44, indicating low blood solubility for these gases.[15]

Human exposures to propane were consistent with the model predictions for narcosis onset and speed of action. Humans exposed at 1,000 ppm (0.1%) propane for 10 minutes did not experience any CNS symptoms, while those exposed at 100,000 ppm (10%) experienced distinct vertigo in 2 minutes.[26] These data indicated that the onset of narcosis for propane exposures occurred at a concentration between 1,000 and 100,000 ppm (e.g., possibly at 47,000 ppm as predicted by the model) and occurs quickly (under 15 minutes). Consistency between the model predictions for narcosis onset and speed of action and human exposure were seen clearly with another hydrocarbon gas, butane. Humans exposed at 10,000 ppm (1%) of butane for 10 minutes reported dizziness.[26] The Drummond model predicted narcosis onset (which includes dizziness) would occur at 17,000 ppm of butane in less than 15 minutes.

The model also predicted narcosis onset would be, respectively, at 300,000, 130,000, 47,000, and 17,000 ppm for methane, ethane, propane, and butane. This indicated that, at the lower explosive

limit (LEL) for methane (50,000 ppm), ethane (30,000 ppm), and propane (21,200 ppm), these substances would not be narcotic.[15] However, at concentrations near the LEL (18,600 ppm), butane will induce narcosis.[15] Further, mixtures of hydrocarbon gases can contribute to CNS depression or intoxication at levels below the LEL.[15]

Cardiac Sensitization

Propane, butane, and isobutane were considered weak cardiac sensitizers in humans following inhalation exposures at high concentrations (e.g., >5% isobutane; >10% propane).[10,12] However, exposures to up to 1000 ppm isobutane and a mixture of isobutane and propane (approximately 500 ppm and 100 ppm, respectively) did not produce sensitization or any ECG abnormality.[24] Exposure-related cardiac sensitization in humans in the workplace is difficult to assess. Past experience in anesthesiology indicated that compounds producing cardiac sensitization in dogs also produced it in humans.[12]

Cardiac sensitization[12] can occur when high concentrations of hydrocarbon sensitizers were inhaled in the presence of elevated epinephrine (e.g., during anxiety, exertion) and possibly during conditions of hypoxia. Cardiac sensitization is characterized by a sudden onset of cardiac arrhythmia (usually ventricular in origin) that may result in sudden death. Cardiac sensitization can occur even with very brief exposures. Siegel and Wason[27] indicated that butane and propane use may represent the most common sudden sniffing death hazard in the United States. They also indicated that sniffing butane lighter fluid was a common practice among many adolescents in U.S., with as many as 20% having experimented with both butane and propane (e.g., Ronson® and Zippo® butane lighter refills and Scotch Guard®). In addition, these researchers reported that 100 sudden deaths per year were due to sniffing butane and propane in the United Kingdom. A combination of butane, isobutane, and propane were detected in the blood, brain, and lung tissue, generally highest in the brain, among those who succumbed. Based on the history, sudden death was presumed to be through a cardiac dysrhythmia mechanism.

In humans, many unexpected or sudden deaths due to ventricular fibrillation have occurred, including at least 20 deaths where propane (and propylene) was found in body tissues.[4] The first human case report of ventricular tachycardia associated with an accidental exposure of a 2-year-old child to isobutane, n-butane, and propane via deodorant was by Wason et al.[28] Significant exposure was confirmed by the presence of n-butane and isobutane in serum. The authors considered the life-threatening seizures to be consistent with CNS stimulation by butane and isobutane in the presence of increased epinephrine as precipitating the heart dysrhythmia. Rohrig[29] documented five sudden deaths due to inhalation of butane, isobutane, and propane, which were also thought to be related to cardiac sensitization.

Part of the evidence relating to cardiac sensitization and unexpected death due to sudden ventricular fibrillation was from analogous situations when humans were under stress while exposed to hydrocarbons, e.g., administration of anesthetics, following industrial exposure to compounds such as benzene and trichloroethylene, and aerosol sniffing. Epinephrine levels are likely to be high when the concentration of these hydrocarbon gases is also high. Thus, while the light hydrocarbon gases are weak sensitizers, under stressful conditions and high concentrations, the effects of cardiac sensitization may be important with these hydrocarbon gases. It is theoretically possible that the asphyxiant effects (hypoxia) may enhance the CNS and sensitization effects in a nonlinear fashion.[12]

Human workplace cardiac arrhythmia is difficult to assess. Past experience in anesthesiology indicated that compounds producing cardiac arrhythmia in dogs would also produce it in humans.[12] The mechanism for cardiac arrhythmia may involve a disturbance in the electrical impulse through the heart, due to a local disturbance in the electrical potential across the cell membrane, in the presence of epinephrine.[12] Cardiac arrhythmia can occur when high concentrations of hydrocarbon gases are inhaled when epinephrine is elevated (e.g., anxiety, exertion) and possibly during hypoxic conditions. Cardiac arrhythmia can also occur even with brief exposures, onset can be sudden, and may result in death.[12]

No exposure-related effects were noted in human volunteers after propane exposure at 1,000 ppm for 8 hours[24] or at 250 to 1000 ppm isobutane for 8 hours/day for 10 days.[4] Reinhardt et al.[12] classify propane as a weak cardiac sensitizing agent after a 5-minute exposure at 100,000 ppm (10%) propane. Exposure at 200,000 ppm (20%) propane caused marked responses 58% of the time. Drummond[30] describes three incidents in a gas processing plant where there was high exposure to light hydrocarbon gases resulting in dizziness, disorientation, weakness, inability to walk, and in one case unconsciousness. All three were quickly removed from exposure but complained of headache, nausea, and weakness. None were aware of any unusual conditions. In one of the incidents, the concentration of the hydrocarbon mixture was about 6000 ppm, measured as methane, a level clearly inadequate to cause asphyxiation.

TLV Recommendation

A TLV–TWA of 1000 ppm is recommended for all C_1 to C_4 alkane hydrocarbon gases. This limit

applies to individual gases (methane, ethane, propane, butane, isobutane) and mixtures of these gases, to include LPG and natural gas, and is believed to be protective against potential health effects that include CNS depression[4,15] and cardiac sensitization.[12,29] The TLV is based upon the abilities of these gases to produce weak depressant effects on the CNS at high concentration levels approaching the lower flammability limit. It has also been reported that ethane and propane can induce cardiac arrhythmias under certain conditions leading to ventricular fibrillation which can result in death in the presence of high epinephrine levels.[12] This recommendation is based on good industrial hygiene practice and on a review of the scientific evidence documenting the toxicological effects of methane, ethane, propane, and butane.[4,15] There are no data to suggest the C_1 to C_4 alkane hydrocarbon have a potential to cause cancer or act as a sensitizer, as defined in the Introduction to the Chemical Substances.

TLV Basis/Critical Effect(s)

CNS depression; cardiac sensitization

TLV Chronology

Butane, All isomers

1971–1972: TLV–TWA, none; Simple Asphyxiants (SA) Appendix
1971 *proposed*: TLV–TWA, 500 ppm
1973–1975: TLV–TWA, 500 ppm, SA Appendix
1974 *proposed*: TLV–TWA, 600 ppm
1976–1980: TLV–TWA, 600 ppm, SA Appendix
1976–1980: TLV–STEL, 750 ppm
1979 *proposed*: TLV–TWA, 800 ppm
1981: Removed from SA Appendix
1981–2003: TLV–TWA, 800 ppm
2003 *proposed*: Withdraw adopted Documentation and TLV; *see* Aliphatic hydrocarbon gases

Ethane and Methane

1965–1988: TLV–TWA, none; SA Appendix
1989: SA Appendix, deleted
1989–2003: TLV, none; Simple Asphyxiant, oxygen content to be > 18% by volume; consider explosion hazard
2003 *proposed:* Withdraw status as Simple Asphyxiant; *see* Aliphatic hydrocarbon gases

Liquified Petroleum Gas

1964: *proposed:* TLV–TWA, 1000 ppm
1966–2003: TLV–TWA, 1000 ppm
1976–1986: TLV–STEL, 1250 ppm
1985 *proposed:* Withdraw TLV–STEL
1987: TLV–STEL withdrawn
2003 *proposed*: Withdraw adopted Documentation and TLV; see Aliphatic hydrocarbon gases

Propane

1964 *proposed:* TLV–TWA, 1000 ppm
1966–1967: TLV–TWA, 1000 ppm
1968–1969: TLV–TWA, 1000 ppm; SA Appendix
1970: TLV–TWA, 1000 ppm withdrawn
1970–1988: TLV, none; SA Appendix
1989: SA Appendix deleted
1989–1997: TLV, none; Simple asphyxiant; oxygen content to be 18%; consider explosion hazard
1996 *proposed:* TLV–TWA, 2500 ppm
1998–2003: TLV–TWA, 2500 ppm
2003 *proposed:* Withdraw adopted Documentation and TLV; see Aliphatic hydrocarbon gases

Aliphatic Hydrocarbon Gases: Alkanes [C_1–C_4]

2003 *proposed*: TLV–TWA, 1000 ppm
2004: TLV–TWA, 1000 ppm

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Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL *	Notations	MW	TLV® Basis
Acetaldehyde [75-07-0] (1992)	—	C 25 ppm	A3	44.05	Eye & URT irr
Acetic acid [64-19-7] (2003)	10 ppm	15 ppm	—	60.00	URT & eye irr; pulm func
Acetic anhydride [108-24-7] (1990)	5 ppm	—	—	102.09	Eye & URT irr
Acetone [67-64-1] (1998)	500 ppm	750 ppm	A4; BEI	58.05	URT & eye irr; CNS impair; hematologic eff
Acetone cyanohydrin [75-86-5], as CN (1991)	—	C 5 mg/m³	Skin	85.10	URT irr; headache; hypoxia/cyanosis
Acetonitrile [75-05-8] (1996)	20 ppm	—	Skin; A4	41.05	LRT irr
Acetophenone [98-86-2] (1990)	10 ppm	—	—	120.15	Eye irr
Acetylene [74-86-2] (1990)		Simple asphyxiant (D)		26.02	Asphyxia
Acetylsalicylic acid (Aspirin) [50-78-2] (1977)	5 mg/m³	—	—	180.15	Skin & eye irr
Acrolein [107-02-8] (1995)	—	C 0.1 ppm	Skin; A4	56.06	Eye & URT irr; pulm edema; pulm emphysema
Acrylamide [79-06-1] (2003)	0.03 mg/m³ (IFV)	—	Skin; A3	71.08	CNS impair
Acrylic acid [79-10-7] (1986)	2 ppm	—	Skin; A4	72.06	URT irr
Acrylonitrile [107-13-1] (1997)	2 ppm	—	Skin; A3	53.05	CNS impair; LRT irr

Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL	Notations	MW	TLV® Basis
Adipic acid [124-04-9] (1990)	5 mg/m³	—	—	146.14	URT irr; ANS impair
Adiponitrile [111-69-3] (1990)	2 ppm	—	Skin	108.10	URT & LRT irr
* Alachlor [15972-60-8] (2006)	1 mg/m³ (IFV)	—	SEN; A3	269.8	Hemosiderosis
* Aldrin [309-00-2] (2006)	0.05 mg/m³ (IFV)	—	Skin; A3	364.93	CNS impair; liver & kidney dam
Aliphatic hydrocarbon gases					
Alkane [C_7–C_8] (2001)	1000 ppm	—	—	Varies	Card sens; CNS impair
Allyl alcohol [107-18-6] (1996)	0.5 ppm	—	Skin; A4	58.08	Eye & URT irr
Allyl chloride [107-05-1] (1990)	1 ppm	2 ppm	A3	76.50	Eye & URT irr; liver & kidney dam
Allyl glycidyl ether (AGE) [106-92-3] (1995)	1 ppm	—	A4	114.14	URT irr; dermatitis; eye & skin irr
Allyl propyl disulfide [2179-59-1] (2001)	0.5 ppm	—	SEN	148.16	URT & eye irr
‡ (Aluminum [7429-90-5] and compounds, as Al)					(LRT irr)
(Metal dust)	(10 mg/m³)	—	—	(26.98)	
(Pyro powders)	(5 mg/m³)	—	—	(Varies)	
(Soluble salts)	(2 mg/m³)	—	—	(Varies)	
(Alkyls (NOS))	(2 mg/m³)	—	—	(Varies)	
‡ (Aluminum oxide [1344-28-1])	(10 mg/m³ (R))	—	(A4)	(101.96)	(LRT irr; pneumoconiosis)

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Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL	Notations	MW	TLV® Basis
Benzene [71-43-2] (1996)	0.5 ppm	2.5 ppm	Skin; A1; BEI	78.11	Leukemia
Benzidine [92-87-5] (1979)	— (L)	—	Skin; A1	184.23	Bladder cancer
Benzo[b]fluoranthene [205-99-2] (1990)	— (L)	—	A2; BEI_P	252.30	Cancer
Benzo[a]pyrene [50-32-8] (1990)	— (L)	—	A2; BEI_P	252.30	Cancer
Benzotrichloride [98-07-7] (1994)	—	C 0.1 ppm	Skin; A2	195.50	Eye, skin, & URT irr
Benzoyl chloride [98-88-4] (1992)	—	C 0.5 ppm	A4	140.57	URT & eye irr
Benzoyl peroxide [94-36-0] (1990)	5 mg/m³	—	A4	242.22	URT & skin irr
Benzyl acetate [140-11-4] (1990)	10 ppm	—	A4	150.18	URT irr
Benzyl chloride [100-44-7] (1990)	1 ppm	—	A3	126.58	Eye, skin, & URT irr
‡ Beryllium [7440-41-7] and compounds, as Be	(0.002 mg/m³)	(0.01 mg/m³)	(—); A1	9.01	(Cancer (lung); berylliosis)
Biphenyl [92-52-4] (1979)	0.2 ppm	—	—	154.20	Pulm func
Bis (2-dimethylaminoethyl) ether (DMAEE) [3033-62-3] (1997)	0.05 ppm	0.15 ppm	Skin	160.26	URT, eye, skin irr
Bismuth telluride (1970)				800.83	Lung dam
Undoped [1304-82-1]	10 mg/m³	—	A4		
Se-doped, as Bi_2Te_3	5 mg/m³	—	A4		

Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL	Notations	MW	TLV® Basis
Borate compounds, inorganic [1330-43-4; 1303-96-4; 10043-35-3; 12179-04-3] (2004)	2 mg/m³ (I)	6 mg/m³ (I)	A4	Varies	URT irr
Boron oxide [1303-86-2] (1985)	10 mg/m³	—	—	69.64	Eye & URT irr
Boron tribromide [10294-33-4] (1990)	—	C 1 ppm	—	250.57	URT irr
Boron trifluoride [7637-07-2] (1962)	—	C 1 ppm	—	67.82	LRT irr; pneumonitis
Bromacil [314-40-9] (1976)	10 mg/m³	—	A3	261.11	Thyroid eff
Bromine [7726-95-6] (1991)	0.1 ppm	0.2 ppm	—	159.81	URT irr; lung dam; LRT irr
Bromine pentafluoride [7789-30-2] (1979)	0.1 ppm	—	—	174.92	Eye, skin, & URT irr
Bromoform [75-25-2] (1988)	0.5 ppm	—	Skin; A3	252.80	URT irr; liver dam
1-Bromopropane [106-94-5] (2003)	10 ppm	—	—	122.99	Liver dam; embryo/fetal dam; neurotoxicity
1,3-Butadiene [106-99-0] (1994)	2 ppm	—	A2	54.09	Cancer
Butane, All isomers [106-97-8; 75-28-5]	*See* Aliphatic hydrocarbon gases: Alkane [C_1—C_4]				
n-Butanol [71-36-3] (1998)	20 ppm	—	—	74.12	Eye & URT irr
sec-Butanol [78-92-2] (2001)	100 ppm	—	—	74.12	URT irr; CNS impair

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Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL	Notations	MW	TLV® Basis
Phorate [298-02-2] (2002)	0.05 mg/m³ (IFV)	—	Skin; A4; BEI_A	260.40	Cholinesterase inhib
Phosgene [75-44-5] (1992)	0.1 ppm	—	—	98.92	URT irr; pulm edema; pulm emphysema
Phosphine [7803-51-2] (1992)	0.3 ppm	1 ppm	—	34.00	URT irr; headache; GI irr; CNS impair
Phosphoric acid [7664-38-2] (1992)	1 mg/m³	3 mg/m³	—	98.00	URT, eye, & skin irr
Phosphorus (yellow) [12185-10-3] (1992)	0.1 mg/m³	—	—	123.92	LRT, URT, & GI irr; liver dam
Phosphorus oxychloride [10025-87-3] (1979)	0.1 ppm	—	—	153.35	URT irr
Phosphorus pentachloride [10026-13-8] (1985)	0.1 ppm	—	—	208.24	URT & eye irr
Phosphorus pentasulfide [1314-80-3] (1992)	1 mg/m³	3 mg/m³	—	222.29	URT irr
Phosphorus trichloride [7719-12-2] (1992)	0.2 ppm	0.5 ppm	—	137.35	URT, eye, & skin irr
Phthalic anhydride [85-44-9] (1992)	1 ppm	—	SEN; A4	148.11	URT, eye, & skin irr
m-Phthalodinitrile [626-17-5] (1974)	5 mg/m³	—	—	128.14	Eye & URT irr
Picloram [1918-02-1] (1992)	10 mg/m³	—	A4	241.48	Liver & kidney dam
Picric acid [88-89-1] (1992)	0.1 mg/m³	—	—	229.11	Skin sen; dermatitis; eye irr
Pindone [83-26-1] (1992)	0.1 mg/m³	—	—	230.25	Coagulation

Substance [CAS No.] (*Documentation* date)	ADOPTED VALUES TWA	STEL	Notations	MW	TLV® Basis
Piperazine dihydrochloride [142-64-3] (1992)	5 mg/m³	—	—	159.05	Eye & skin irr; skin sen; asthma
Platinum [7440-06-4] (1979)					
Metal	1 mg/m³	—	—	195.09	Asthma; URT irr
Soluble salts, as Pt	0.002 mg/m³	—	—	Varies	Asthma; URT irr
‡ Portland cement [65997-15-1] (1992)	(10 mg/m³ (E))	(—)	(—)	—	(Irr; dermatitis)
Potassium hydroxide [1310-58-3] (1992)	—	C 2 mg/m³	—	56.10	URT, eye, & skin irr
Propane [74-98-6]	*See* Aliphatic hydrocarbon gases: Alkane [C_1—C_4]				
Propane sultone [1120-71-4] (1976)	— (L)	—	A3	122.14	Cancer
* n-Propanol (n-Propyl alcohol) [71-23-8] (2006)	100 ppm	—	A4	60.09	Eye & URT irr
2-Propanol [67-63-0] (2001)	200 ppm	400 ppm	A4	60.09	Eye & URT irr; CNS impair
Propargyl alcohol [107-19-7] (1992)	1 ppm	—	Skin	56.06	Eye irr; liver & kidney dam
β-Propiolactone [57-57-8] (1992)	0.5 ppm	—	A3	72.06	Skin cancer; URT irr
Propionaldehyde [123-38-6] (1998)	20 ppm	—	—	58.1	URT irr
Propionic acid [79-09-4] (1977)	10 ppm	—	—	74.08	Eye, skin, & URT irr
Propoxur [114-26-1] (1992)	0.5 mg/m³	—	A3; BEI_A	209.24	Cholinesterase inhib

DFG, Occupational Toxicants, vol. 20, 2003.

Butane (both isomers)

MAK value (1966)	**1000 ml/m³ (ppm) ≙ 2400 mg/m³**	
Peak limitation (1983)	**Category II, excursion factor 4**	
Absorption through the skin	–	
Sensitization	–	
Carcinogenicity	–	
Prenatal toxicity (1999)	**see Section IIc of the *List of MAK and BAT Values***	
Germ cell mutagenicity	–	
BAT value	–	
Synonyms	*n*-butane	isobutane
Chemical name (CAS)	butane	2-methylpropane
CAS number	106-97-8	75-28-5
Structural formula	$H_3C–(CH_2)_2–CH_3$	$(H_3C)_3CH$
Molecular formula	C_4H_{10}	C_4H_{10}
Molecular weight	58.12	58.12
Melting point	–138.4°C	–159.6°C
Boiling point	–0.5°C	–11.7°C
log P_{ow}*	2.89	2.88
1 ml/m³ (ppm) ≙ 2.41 mg/m³	**1 mg/m³ ≙ 0.415 ml/m³ (ppm)**	

The MAK value for the two butane isomers was established in 1966 in analogy to the TLV value at the time. This chapter is based on reviews of the toxicological data for *n*-butane and isobutane (ECB 1995a, 1995b, Low *et al.* 1987, Moore 1982, Sandmeyer 1981).

* n-octanol/water distribution coefficient

1 Toxic Effects and Mode of Action

The butane isomers can be absorbed via inhalation and distributed in the body with the highest level of accumulation in adipose tissue. Dermal penetration may be assumed to be negligible. The main metabolites of *n*-butane are *sec*-butyl alcohol and methyl ethyl ketone, that of isobutane is *tert*-butyl alcohol. There are no data for excretion.

In animal experiments *n*-butane and isobutane were not found to be acutely toxic. Exposure to high concentrations of *n*-butane and isobutane caused central nervous depression or even narcosis. The butane isomers increase the sensitivity of the heart muscle to adrenaline.

n-Butane is not irritative in the eye and respiratory tract of the rabbit, isobutane causes weak to moderate irritation of the rabbit skin. Liquefied *n*-butane and isobutane can cause "chemical freezing" on the skin and in the eye.

Prenatal toxicity is found only as a result of maternal anoxia after exposure of the dams to very high butane concentrations.

The available studies have not shown the butane isomers to be mutagenic.

2 Mechanism of Action

The central nervous depression is probably the result of the lipophilia of the substances and the consequent interaction with neuronal membranes.

The mechanism for the increased sensitivity of the heart muscle to adrenaline after exposure to *n*-butane and isobutane is still unclear.

3 Toxicokinetics and Metabolism

There are no data for the pulmonary retention in man of either *n*-butane or isobutane. The pulmonary absorption rate was determined in male F344 rats exposed nose only to *n*-butane or isobutane concentrations of 1, 10, 100, 1000 and 5000 ml/m^3 daily for 80 minutes on 5 consecutive days. Inhalation of 100 ml/m^3 yielded for *n*-butane a rate of 1.5 to 1.8 nmol/kg body weight and minute per ml/m^3, for isobutane 0.6 nmol/kg body weight and minute per ml/m^3 (Dahl *et al.* 1988).

Studies of the oral and dermal absorption of the two isomers are not available. Because of the high vapour pressure of *n*-butane and the resulting brief contact with the skin, no notable penetration through the skin is to be expected (Low *et al.* 1987).

After inhalation exposure of rats for 4 hours to lethal concentrations of *n*-butane (658000 mg/m^3), the highest concentrations were found in adipose tissue, followed by

the brain, spleen, liver and kidneys. In mice exposed for 2 hours to the likewise lethal concentration of 680000 mg/m^3, the concentration of *n*-butane in the brain was similar to that in the rat brain (Shugaev 1969).

In male ICR mice exposed for one hour to *n*-butane mixed with oxygen in the ratio 200 ml/min to 100 ml/min (resulting in exposure to an estimated 660000 ml/m^3), in addition to unchanged butane, *sec*-butyl alcohol and methyl ethyl ketone were found as the main metabolites in blood and in various organs. After exposure of the mice to isobutane, the main metabolite found was *tert*-butyl alcohol. In this study, the metabolites were identified only qualitatively. Also when *n*-butane and isobutane were incubated with rat liver microsomes and an NADPH-regenerating system, the main metabolites were *sec*-butyl alcohol and *tert*-butyl alcohol (Tsukamoto *et al.* 1985). Further oxidation of *sec*-butyl alcohol to the ketone is catalysed by alcohol dehydrogenase (Tsukamoto *et al.* 1985). *tert*-Butyl alcohol is hardly transformed by alcohol dehydrogenase and therefore has a longer biological half-life (DECOS 1994).

4 Effects in Man

The odour threshold for *n*-butane is 50000 ml/m^3 (Sandmeyer 1981).

There are no data available for the allergenic effects of the butane isomers in man, or their genotoxicity and carcinogenicity.

4.1 Single exposures

The threshold concentration for central nervous effects is not known exactly for either of the butane isomers.

Exposure of 8 volunteers to isobutane concentrations between 250 and 1000 ml/m^3 for up to 8 hours did not produce subjective or clinical symptoms. A series of investigations did not find effects on the heart, lungs, central nervous system, blood or urine (Stewart *et al.* 1977).

Exposure for 10 minutes to *n*-butane concentrations of 10000 ml/m^3 did not induce systemic effects other than dizziness (no other details; Sandmeyer 1981).

On the basis of the solubility of the substance in olive oil and the distribution coefficient between air and olive oil, a narcotic concentration of 17000 ml/m^3 was estimated for *n*-butane and of 24000 ml/m^3 for isobutane (Drummond 1993).

Butane is often inhaled intentionally to produce inebriation. The number of deaths resulting from such misuse of butane and propane in young people has increased in recent years. Butane and propane consumption are probably the most frequent cause of death from sniffing in the USA (Siegel and Wason 1997).

There are a few case reports in which the symptoms of massive over-exposure were documented. After inhaling an unknown amount of butane gas from a canister, a 15-year-old boy developed right hemiparesis, characterized by massive loss of muscle strength in the upper and lower extremities, reduced muscle tone and lacking plantar reflexes of the extensors. The computer-assisted tomogram of the central nervous system did not reveal pathological findings (such as cerebral infarction). The symptoms had improved markedly by the time he was discharged after five days stationary care, but the patient still suffered from muscle weakness in the upper extremities and had a hemiplegic gait (Gray and Lazarus 1993). In another case, a 16-year-old boy suffered cardiac arrest after inhaling butane gas (level of exposure unknown). The ECG revealed an incomplete right bundle-branch block with anterolateral ST-segment elevation and T wave inversion. The patient recovered after intensive care, but for 24 days had a memory gap for the period before his unconsciousness. The mechanism that induced the cardiac arrest was not discovered. The authors mentioned as possible mechanisms general cerebral depression and, associated with this, anoxia and ventricular flutter which resulted in asystole, or the direct induction of asystole by butane (Roberts *et al.* 1990). From animal studies it is known that the butane isomers can have arrhythmogenic effects as a result of sensitization of the heart to catecholamines (see Section 5.1).

The inhalation of unknown amounts of butane gas led to the deaths of 4 other persons. In three of the four cases, *n*-butane or isobutane or a mixture of *n*-butane, isobutane and propane were detected in the blood, brain and lungs. In the fourth case, the time of inhalation was long past and analysis no longer seemed worthwhile. After inhalation of a spray containing *n*-butane (no other details) another person suffered respiratory arrest and died. The largest amount of the hydrocarbons was detected in the brain in all cases. The author suspected in all 5 cases disturbances in heart rhythm to be the cause of death (Rohrig 1997).

4.2 Repeated exposures

In volunteers exposed to isobutane concentrations of 500 ml/m^3 for up to 8 hours, 5 days a week for 2 weeks, no clinical symptoms associated with the exposure could be detected. Likewise, no effects were observed in the ECG, the EEG, in spirometric examinations, in cognitive tests or in the blood and urine analyses. In the second week, a reduction in visually evoked potentials was found in the volunteers, which, according to the authors, may have been the result of CNS depression, but still needs clarification (Stewart *et al.* 1977).

22 workers from a liquid gas filling station (propane and butane), who were exposed to a maximum of 0.8 volume parts gas (8000 ml/m^3) (measurements carried out on two occasions), reported symptoms such as a dry throat, a dry cough, severe agitation and sometimes dizziness. ECG examination of the workers revealed tachycardia, extrasystoles and incomplete right bundle-branch block (no other details; BUA 1994, ECB 1995a, 1995b).

Of 12 persons who repeatedly inhaled butane gas for inebriation, most reported the development of euphoria and hallucinations (Evans and Raistrick 1987).

4.3 Local effects on skin and mucous membranes

Gaseous isobutane does not have irritative effects on the skin or eyes. As a result of evaporative cooling, liquefied *n*-butane and isobutane can cause "chemical freezing" on the skin and in the eye (Sandmeyer 1981).

4.4 Reproductive and developmental toxicity

A woman who suffered severe intoxication with butane gas in week 27 of gestation (no other details), gave birth to a child with hydranencephaly. The authors suspect that the malformation was caused by intrauterine anoxia during development of the foetal brain (Fernàndez *et al.* 1986). A woman who attempted suicide with butane gas in week 30 of gestation, gave birth to a child that died 11 hours after the birth. Severe multi-cystic encephalomalacia was diagnosed. Also in this case, it was not a substance-specific effect of butane gas, but damage caused by maternal anoxia (BUA 1994).

5 Animal Experiments and *in vitro* Studies

5.1 Acute toxicity

According to studies with single exposures, the acute toxicity of *n*-butane and isobutane is very weak. The LC_{50} of *n*-butane for rats after exposure for 4 hours was found to be 658000 mg/m^3 (273000 ml/m^3), for mice after exposure for 2 hours 680000 mg/m^3 (282000 ml/m^3) (Shugaev 1969). Exposure of mice to 130000 ml/m^3 for 25 minutes or to 220000 ml/m^3 for 1 minute produced narcotic effects (BUA 1994). The exposure of dogs to *n*-butane concentrations of 150000 to 900000 ml/m^3 for 10 minutes caused sensitization of the heart muscle to adrenaline-induced cardiac irregularity (Low *et al.* 1987).

The LC_{50} of isobutane for mice exposed for 2 hours was found to be 520000 ml/m^3 (Low *et al.* 1987). Close to the LC_{50}, CNS depression, rapid and shallow breathing, and apnoea were observed in mice (Sandmeyer 1981). The LC_{50} for rats exposed for 15 minutes was found to be 570000 ml/m^3, the EC_{50} for central nervous effects caused by exposure for 10 minutes was given as 200000 ml/m^3 (BUA 1994). Narcotic effects were observed in mice after exposure to isobutane concentrations of 150000 ml/m^3 for 60 minutes or 230000 ml/m^3 for 26 minutes. Exposure to concentrations of 450000 ml/m^3 for 10 minutes caused narcosis in dogs (Sandmeyer 1981). The EC_{50} for heart muscle sensitization to adrenaline caused by exposure for 5 minutes was found to be 70000 ml/m^3 for the dog (BUA 1994).

In 3 anaesthetized and intubated rhesus monkeys with opened thoraxes, arrhythmia and myocardial depression were observed after inhalation of isobutane concentrations of