Table 9. Pulmonary function after 6 hr exposure to fluorocarbon-11.[a]

Condition	FVC, l. BTPS	$\frac{FEV_1}{FVC}$, %	PEFR, l./sec	MMEF, l./sec
Repetitive exposure F-11, 1000 ppm, $n = 8$				
Control	5.94	80.6	11.41	4.92
	0.6	5.6	0.7	0.4
4th day, 1st wk	5.76	82.4	11.47	5.09
	0.5	9.1	0.5	0.7
	6.12	81.1	11.73	5.01
4th day, 2nd wk.	0.7	6.2	0.3	0.6
4th day, 3rd wk	6.26	81.1	12.02	5.20
	0.4	4.1	0.6	0.6
4th day, 4th wk	5.81	81.1	11.41	5.10
	0.7	5.1	0.4	0.5
Single exposure F-11, 1000 ppm, $n = 7$				
Control	4.76	76.1	9.08	4.32
	0.4	9.1	0.5	0.7
Single exposure	4.87	74.5	9.81	4.45
	0.7	11.0	0.3	1.1

[a] Pulmonary function: FVC = maximum volume of air exhaled after a maximum inspiration; FEV_1/FVC = per cent of FVC exhaled in 1 sec; PEFR = maximum rate of air flow during FVC maneuver; MMEF = maximum rate of air flow at midpoint of FVC.

Electroencephalography

No significant alterations occurred in the EEGs of any of the subjects under any of the exposure conditions. Time constraints precluded the obtaining of a complete EEG, thus limiting the value of these data. Actual EEG tracings are reproduced in the three project reports (*16–18*).

Visual Evoked Response

The visual evoked responses recorded during the single exposures were remarkedly reproducible and did not indicate any changes attributable to acute exposure to the four propellants at the concentrations studied.

During the repetitive exposures the only significant VER changes observed occurred during the second week of exposure to 500 ppm isobutane During this period a definite reduction in wave amplitude was observed. Representative VER tracings are presented in the three project reports (*16–18*).

Cognitive Tests

With the exception of F-11, exposure to the propellants or to mixtures of propellants did not result in cognitive test performance decrements. The eight male subjects repetitively exposed to F-11 did show statistically significant decrements in cognitive test performance (*16*).

The mean test performances under control and exposure conditions were plotted for each control and exposure day. Then a linear regression line with 75% confidence limits was drawn through the 0 ppm data. After adjusting for the trend through the 0 ppm data, *t*-tests were performed to determine if the exposure data were significantly different from the regression line. The results of these *t*-tests are presented in both graphic and tabular form in the three project reports (*16–18*).

Sporadic individual improvement or decrement in test performance was observed from time to time. However, in the absence of a consistent decrement in test performance or a dose-related response, the test results are interpreted as showing no effect of exposure at the concentrations studied.

ACTH Stimulation Test

Following the repetitive exposures the subjects had normal 24 hr urinary 17-ketosteroid and 17-hydroxyketosteroid excretion. The subjects given an 8 hr ACTH stimulation test (40 units) on two successive days showed a normal response (*16–18*).

Table 10. Pulmonary function after 6 hr exposure to fluorocarbon-12.[a]

Condition	FVC, l. BTPS	$\frac{FEV_1}{FVC}$, %	PEFR, l./sec	MMEF, l./sec
Repetitive exposure F-12, 1,000 ppm, $n = 8$				
Control	5.84 ± 0.6	80.6 ± 5.6	11.41 ± 0.7	4.92 ± 0.4
4th day, 1st wk	5.89 ± 0.5	82.6 ± 6.1	11.51 ± 0.5	4.97 ± 0.7
4th day, 2nd wk	5.85 ± 0.7	83.2 ± 6.2	11.27 ± 0.3	5.13 ± 0.6
4th day, 3rd wk	5.85 ± 0.4	82.5 ± 5.1	11.46 ± 0.6	4.92 ± 0.6
4th day, 4th wk	5.62 ± 0.5	84.9 ± 4.1	11.42 ± 0.4	5.05 ± 0.5
Single exposure F-12, 1000 ppm $n = 7$ males				
Control	4.76 ± 0.4	76.1 ± 9.1	9.08 ± 0.5	4.32 ± 0.7
Single exposure	4.77 ± 0.7	78.5 ± 10.6	9.72 ± 0.6	4.55 ± 0.8
Single exposure F-12, 1000 ppm, $n = 4$ females				
Control	4.10 ± 0.7	78.2 ± 6.1	8.93 ± 0.5	5.10 ± 0.7
Single exposure	4.00 ± 0.5	76.7 ± 9.2	9.10 ± 0.6	4.85 ± 0.6

[a] Pulmonary function: FVC = maximum volume of air exhaled after a maximum inspiration; FEV_1/FVC = percent of FVC exhaled in 1 sec; PEFR = maximum rate of air flow during FVC maneuver, MMEF = maximum rate of air flow at midpoint of FVC.

Breath Analysis

Isobutane, propane, F-12, and F-11 were readily detected in the expired breath of each of the subjects following exposure to the concentrations investigated. These post-exposure breath data are detailed in the project reports (*16–18*). Examination of these breath data reveals that a predictable excretion pattern exists for each of the exposure conditions studied, and that the following factors influence the concentration of the propellant in the breath: concentration of inspired gas or vapor, duration of exposure, and length of time post-exposure that the breath sample is obtained. From the data presented a "family" of post-exposure breath excretion curves useful in estimating the magnitude of exposure can be constructed (*16–18*).

Blood Analysis

Isobutane, propane, F-12, and F-11 were present in detectable concentrations in the blood of the subjects exposed under the conditions of this experiment. However, the sensitivity of the analytic method severely limits the usefulness of this technique for monitoring the body burden except in the early post-exposure interval (*16–18*).

Comments

Acute exposures to isobutane, propane, F-12, and F-11 in concentrations of 250, 500, or 1000 ppm for periods of 1 min to 8 hr did not produce any untoward physiological effects as monitored by the methods employed. Repetitive exposures to these four propellants were also without measurable untoward physiological effect with the exception of the eight male subjects repetitively exposed to 1000 ppm F-11, who did show minor decrements in several of the cognitive tests. Should these observations prove representative of the general population, a significant percentage of persons identically exposed to the upper industrial limits of F-11 would be expected to show similar decrements in cognitive function. Fortunately, the magnitude of the decrements observed was minute and transient. In the opinion of the investigators, these small decrements occurring during repetitive exposures were spurious in that similar decrements were not observed in the subjects acutely exposed to the same concentration for equal periods of time. Further research on the effect of F-11 on cognitive function is merited.

Of particular importance is the observation that none of the subjects showed any decrement in pulmonary function or alteration in cardiac rhythm as the result of exposure to concentrations of the gases or vapors far higher and of much greater duration than would occur in the normal use of commercial aerosols in the home. Thus, it would seem that exposure to the current Threshold Limit Value (TLV) for American industry does not have the potential to adversely affect a normal heart or lungs.

These extended observations fail to corroborate the speculation of Speizer et al., who performed less comprehensive studies and suggested that brief exposures to fluorocarbons could result in the development of cardiac arrhythmias (*11*).

The analysis of expired breath for isobutane, propane, F-12, or F-11 in the early post-exposure period provides a feasible diagnostic test of exposure. The use of gas chromatography permits the detection of the gases or vapors for at least 5 hr after exposure to the TLV. Serial breath analyses following exposure provides a means to estimate the magnitude of exposure since the amount of a gas present following exposure is determined by the inspired concentration, the duration of exposure, and the elapsed time following exposure.

Summary

Acute exposures to isobutane, propane, F-12, and F-11 in concentrations of 250, 500, or 1000 ppm for periods of 1 min to 8 hr did not produce any untoward physiological effects as determined by the methods employed which included serial EKGs and continuous monitoring of modified V_5 by telemetry during exposure. Repetitive exposures to these four propellants were also without measurable untoward physiological effect with the exception of the eight male subjects repetitively exposed to 1000 ppm F-11, who did show minor decrements in several of the cognitive tests. Of particular importance is the observation that none of the subjects showed any decrement in pulmonary function or alteration in cardiac rhythm as the result of exposure to concentrations of the gases or vapors far greater than encountered in the normal use of aerosol products in the home.

This investigation was supported in part from funds collected by the Ad Hoc Aerosol Committee, representatives of major trade associations, and industrial companies with interests in aerosol safety.

REFERENCES

1. Bass, M. Sudden sniffing death. J. Am. Med. Assoc. 212: 2075 (1970).
2. Reinhardt, C. F., et al. Cardiac arrhythmias and aerosol "sniffing." Arch Environ. Health, 22: 265 (1971).
3. Clark, D. G., and Tinston, D. J. The influence of fluorocarbon propellants on the arrhythmogenic activities of adre-

naline and isoprenaline in conscious dogs. Proc. Eur. Soc. Study Drug Toxicity, 13: 212 (1972).
4. Clark, D. G., and Tinston, D. J. Sniffing syndrome. Brit. Med. J. 2: 113 (1971).
5. Clark, D. G., and Tinston, D. J. Cardiac effects of isoproterenol, hypoxia, hypercapnia and fluorocarbon propellants and their use in asthma inhalers. Ann. Allergy 30: 536 (1972).
6. Jack, D. Sniffing syndrome, Brit. Med. J. 2: 708 (1971).
7. Taylor, G. J., and Harris, W. S. Cardiac toxicity of aerosol propellants. J. Am. Med. Assoc. 214: 81 (1970).
8. Editorial. Cardiac toxicity of aerosol propellants. J. Am. Med. Assoc. 214: 136 (1970).
9. Azar, A. Cardiac toxicity of aerosol propellants. J. Am. Med. Assoc. 215: 1501 (1971).
10. Zuskin, E., and Bouhuys, A. Acute airway responses to hair-spray preparations. N. Eng. J. Med. 290: 660 (1974).
11. Speizer, F. E., Wegman, D. H., and Ramirez, A. Palpitation rates associated with fluorocarbon exposure in hospital setting. N. Engl. J. Med. 292: 624 (1975).
12. Stewart, R. D. Use of human volunteers for the toxicological evaluation of materials. Paper presented at Symposium on an Appraisal of Halogenated Fire Extinguishing Agents, National Academy of Sciences, Washington, D. C., 1972.
13. Stewart, R. D., et al. Measurement of physiological and behavioral responses in a controlled-environment chamber. In: Behavioral Toxicology: Early Detection of Occupational Hazards, C. Xintaras, B. L. Johnson, and I. de Groot, Eds., HEW Publication No. (NIOSH) 74-126, Washington, D. C., 1974, p. 361.
14. Stewart, R. D., et al. Effect of carbon monoxide on time perception. Arch. Environ. Health 27: 155 (1973).
15. Weissler, A. M., Harris, W. S., and Schoenfeld, C. D. Bedside techniques for the evaluation of ventricular function in man. Am. J. Cardiol. 23: 577 (1969).
16. Stewart, R. D., et al. Acute and repetitive human exposure to fluorotrichloromethane. NTIS Rept. No. PB 279203/LLC, December 1, 1975, National Clearinghouse for Federal Scientific and Technical Information, Springfield, Va.
17. Stewart, R. D., et al. Acute and repetitive human exposure to difluorodichloromethane. NTIS Rept. No. PB 279204/LLC, April, 1976, National Clearinghouse for Federal Scientific and Technical Information, Springfield, Va.
18. Stewart, R. D., et al. Acute and repetitive human exposure to isobutane and propane. NTIS Rept. No. PB 279205 LLC, April, 1977, National Clearinghouse for Federal Scientific and Technical Information, Springfield, Va.
19. Stewart, R. D. The use of breath analysis in clinical toxicology. In: Essays in Toxicology, W. Hayes, Ed., Vol. V., Academic Press, New York, 1974, Chapt. 5.

ISOBUTANE

CAS# 75-28-5

Jennifer B. Galvin, Ph.D., DABT, CIH

Director of Risk Assessment and Toxicology, Phillips Petroleum Co., Bartlesville, Oklahoma, USA

Gary Bond, Ph.D., DABT

Toxicologist, Phillips Petroleum Co., Bartlesville, Oklahoma, USA

Isobutane is a relatively stable low molecular weight alkane and is a flammable gas. It is inert to most chemical reagents (Expert Panel, 1982). It has been detected in urban atmospheres (Altshuller & Bellar, 1963) at very low concentrations of 44 to 74 ppb (Gordon et al., 1968). It has been measured in diesel exhaust at 1.4 to 11 ppm (Battigelli, 1963; Altshuller et al., 1971) and in cigarette smoke at 10 ppm (Patton & Touey, 1965). It also evolves from natural sources. Isobutane occurs in small quantities in natural gas and petroleum crude oil, and is produced in refinery processes. Isobutane is used as a raw material for petrochemicals, aerosol propellants, industrial carrier gas, and as a fuel source. It represents one of the basic raw materials used in the chemical industry for the production of propylene glycols, oxides, and polyurethane foams and resins. Isobutane has extensive applications that include use in or as aerosol propellants, aviation fluid additives, industrial and household fuel, blowing agents, solvents, and refrigerants, and is a Generally Recognized As Safe (GRAS) food ingredient (Expert Panel, 1982).

Isobutane is nontoxic except at very high concentrations exceeding the lower flammability limit. Therefore, the hazard due to flammability is reached before that of toxicity. The toxic properties of isobutane are not manifest until exposure levels are reached that exceed the minimum fire hazard concentrations. The lower flammability limit of isobutane is 1.8 vol% in air which is 18,000 ppm. None of the toxic effects reported in the biomedical literature occur at levels below 18,000 ppm.

Only very high vapor concentrations of isobutane produce alterations in normal body functions. No permanent alterations in body function are induced by isobutane. Eliminating exposure to isobutane vapors allows the body to completely recover to normal. Asphyxiation occurs when the concentration of isobutane is sufficient to reduce the amount of oxygen available.

Address correspondence to Jennifer B. Galvin, PhD, DABT, CIH, Manager, Risk Assessment and Toxicology, Phillips Petroleum Company, 12 A1 Phillips Building, Bartlesville, OK 74004, USA. E-mail: jbga@ppco.com

Journal of Toxicology and Environmental Health, Part A, 58:3–22, 1999

0098-4108/99 $12.00 + .00

The low toxicity of isobutane has led to the Food and Drug Administration designation of Generally Recognized As Safe (GRAS) for isobutane and its use as a food ingredient. Isobutane's GRAS status permits its use as a direct food additive under the Food and Drug Administration (FDA) regulations 21 CFR 184.1165. Isobutane may be used as a propellant, as an aerating agent, and as a gas in food at levels not to exceed current good manufacturing practice.

Isobutane is used by the food industry as an aerosol in food products. One manufacturer reported that isobutane makes up 16.8% of a frying pan lubricant (also containing 3.2% propane). Two other frying pan lubricants contain 10 and 16% isobutane. Evidently, manufacturers limit the amount of isobutane in these products to about 16% since the aerosol formulations may be flammable at higher isobutane concentrations. However, water-based formulations of aerosol frying pan lubricants may contain 30% isobutane (FASEB, 1979). Regarding the use of isobutane as a propellant in food products consumed by humans, the Bureau of Foods within the FDA, Select Committee on GRAS Substances (FASEB, 1979), concluded, "There is no evidence in the available information on *n*-butane and isobutane that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current or that might reasonably be expected in the future."

The low toxicity of isobutane has led to its use in consumer products such as personal care and cosmetic products. Because of this use, an independent "blue ribbon" panel of experts published in the peer-reviewed literature a review paper (Expert Panel, 1982) on the health and safety aspects of their cosmetic uses. They concluded that "on the basis of the available information, isopentane, isobutane, *n*-butane and propane are considered safe as cosmetic ingredients under present conditions of concentration and use."

Generally, manufacturing using isobutane is done in closed systems for two reasons: (1) to contain the gas, and (2) to protect workers against flammable atmospheres. A closed system is particularly important since the main safety concern is for flammability and explosivity due to its low flashpoint. Safety precautions to avoid flammability or explosion keep exposures well below those levels associated with anesthesia.

The American Conference of Government Industrial Hygienists documentation (ACGIH, 1991) recommends for both butane and isobutane an 8-h threshold limit value (TLV) of 800 ppm time weighted average (TWA). The ACGIH does not have separate standards for butane and isobutane, but covers both chemicals in the same documentation. OSHA has no permissible exposure limit (PEL) for butane or for isobutane. The vacated OSHA 8-h PEL is set at 800 ppm TWA for butane, which is consistent with that of the ACGIH. A limit of 800 ppm protects workers from drowsiness and other narcotic effects.

The saturated light aliphatic hydrocarbons, such as isobutane, have a lower potential for photoreactivity in the atmosphere than many other

classes of chemicals which are more photoreactive. This is because they do not absorb light since they are basically colorless gases or liquids. Because they are less photoreactive, they contribute less to atmospheric pollution such as ground-level smog and ozone formation than many other agents. Concern about ozone depletion in the upper atmosphere and stratosphere has precipitated the banning and phasing out of the environmentally persistent chlorofluorohydrocarbons (Howard et al., 1995; Birch et al., 1995).

Isobutane has an ozone depletion potential (ODP) of zero and a negligible global warming potential (GWP), which means it is environmentally friendly (Mariani & Mersiadis, 1995). Isobutane is not an ozone depleting substance (ODS) as defined in 40 CFR 82.152, nor is it one of the HAPs (hazardous air pollutants) listed in the Clean Air Act Amendment (CAAA) Section 112(b). It is listed as a volatile organic compound (VOC) as defined in 40 CFR 51.100(s).

TOXICOLOGY

Acute Toxicity

Eye Irritation In the rabbit, 0.1 ml hairspray containing 22% isobutane was sprayed into the eye and followed in 4 seconds by irrigation with water. There was no sign of corneal involvement after 1 h. After 1 h there was transient iritis and mild conjunctivitis which cleared shortly (Expert Panel, 1982).

Skin Irritation There are no acute skin irritation studies on isobutane alone because it is a gas. Toxicologically, isobutane vapor exerts no effect on skin and eyes (Clayton & Clayton, 1994). Several formulation mixtures containing from 62 to 89% of isobutane or a isobutane–propane mixture were moderate skin irritants, showing either no to moderate erythema and edema in acute 24-h contact dermal irritation studies in the rabbit (Expert Panel, 1982). Rapid evaporation of the pressurized liquid from the skin leads to a chilling effect, which can cause freeze burn of the skin.

A 12-wk twice daily application of a deodorant and an antiperspirant containing 20 or 21.5% methylene chloride, 64.5 or 70% propane–isobutane aerosol propellant mixture, and 10 or 14% other components produced transient, negligible skin irritation in 125 human volunteers (Meltzer et al., 1977).

Inhalation Isobutane vapor when inhaled is practically nontoxic except at very high concentrations exceeding its lower flammability limit, which is 18,000 ppm. When large quantities are inhaled, isobutane acts as an anesthetic and asphyxiant, which is typical of most light aliphatic petroleum hydrocarbons. At these high levels, alkanes will cause central nervous system (CNS) depression such as drowsiness, anesthesia, and in higher concentrations, coma, and death. The anesthetic activity of isobu-

tane was investigated in mice and dogs. The high concentrations between that required to produce anesthesia and death was found to be narrow.

Mouse The 2-h LC50 for isobutane in the mouse is 52% (520,000 ppm). There were no deaths at 36% (360,000); there was 100% mortality at 65% (650,000 ppm) isobutane (Aviado et al., 1977).

The anesthetic property of isobutane was studied in mice (Stoughton & Lamson, 1936). Inhaled isobutane caused excitement and light anesthesia (CNS depression) at 150,000 ppm for 60 min and at 230,000 ppm for 26 min. Exposure at 350,000 ppm for 25 min proved to be anesthetic, but there were no deaths. The concentration of 410,000 ppm for 3 min caused loss of posture, and exposure for 2 h caused 60% deaths. Surviving mice recovered quickly, on average in 3–4 min, and were normal 2 h following anesthesia. At 500,000 ppm exposure for 2 min isobutane caused loss of posture, and exposure for 2 h was lethal to 100% of the mice within an average of 28 min (Stoughton & Lamson, 1936).

Rat The acute 4-h inhalation LC50 of isobutane in the rat is >13,023 ppm. No test animals died at this concentration. The LC50 is larger than this value of 13,023 ppm, but no measurements were made at a higher concentration to avoid being in the explosive range for isobutane. Albino rats of the Sprague-Dawley strain were exposed to vaporized test material for 4 h at a nominal concentration of 32.21 mg/L (actual concentration 13,023 ppm). The animals were then observed for 14 d. No gross signs and symptoms of intoxication were noted. All animals appeared normal throughout the entire study. Body weights in males were reduced 2 and 3 d postexposure and in females throughout the exposure period (Phillips Petroleum Co., 1982).

Dog Isobutane's anesthetic activity was tested in dogs (Stoughton & Lamson, 1936). In the dog, isobutane is anesthetic at 45% (450,000 ppm) in 10 min. Fifty-five percent (550,000 ppm) was lethal. Administration was directly into the trachea. Stoughton and Lamson said that although not enough experiments were done to give accurate, quantitative results, they found that it was extremely difficult to produce good anesthesia and relaxation with isobutane compared with control experiments with cyclopropane, which were carried out with great ease. None of the butanes and pentanes that they studied gave good anesthesia and relaxation except in concentrations that were practically lethal. Stoughton and Lamson observed that isobutane and isopentane showed less anesthetic activity than their straight-chain homologs, butane and pentane. Isobutane and isopentane were less active than butane and pentane, respectively. They also concluded that the anesthetic activity and lethality of butane was less than that of pentane.

Rabbit Isobutane, at 22% in a hair-setting spray, was not toxic to rabbits in an acute inhalation study (Table 1). The study involved 10 aerosol bursts at 13.2 g/30-s burst (2.90 g isobutane per burst). This is

TABLE 1. Acute Studies in Animals by Noninhalation Routes of Exposure

Species	Conc./route	Study/duration	Effects/references
Rabbit	0.1 ml hairspray with 22% isobutane sprayed into eye	Eye irritation/spray into eye, and after 4 s eye irrigated	After 1-h transient iritis and mild conjunctivitis which soon disappeared; no corneal involvement (CTFA, 1979)
Rabbit	Several formulation mixtures containing from 62–89% of isobutane or a isobutane–propane mixture; skin	Acute dermal irritation study by Consumer Product Safety Commission protocol outlined in 16 CFR 1500.41, 24-h contact	None to moderate erythema and edema; considered mild to moderate irritants (CTFA, 1981)

3575 ppm/burst or 35,750 ppm/10 bursts. No deaths, abnormal behavior, or changes in body weight were observed either during exposure or after 14 d of observation. There were no changes attributed to inhalation in gross or microscopic exams, including respiratory tissues, which were similar to untreated controls (CTFA, 1979).

Pulmonary Irritancy Isobutane did not produce upper airway irritancy in mice breathing 12,460 ppm in a study specifically designed to measure this effect (Phillips Petroleum Co., 1982). The respiratory tract irritancy study involved a head only inhalation exposure in 4 SPF male mice of the CD-1 strain at a nominal concentration to 32.21 mg/L (actual concentration was 12,460 ppm) of isobutane. They were exposed to vaporized test material for 1 min and permitted to recover for 10 min while being exposed to room air only. Following this, the animals were exposed to vaporized test material for 1 min, then to room air for 5 min. During this time their respiratory patterns were continually monitored. There were no patterns of respiratory pauses, and hence, no evidence of respiratory irritancy (Table 2).

Subchronic Toxicity

Kidney damage did not occur in rats breathing mixtures containing isobutane for extended periods of time. Sprague-Dawley rats were exposed by inhalation to various concentrations up to 4437 ppm of a mixture containing 25 wt% each of isobutane, *n*-butane, *n*-pentane, and isopentane for 3 wk, 6 h/d, 5 d/wk. There were no clinical signs of distress, no evidence of kidney lesions, and hematology and clinical chemistry values were within the normal range (Halder et al., 1986).

A 90-d inhalation study was conducted on a 50:50 wt% mixture of isobutane and isopentane. Male and female F344 rats were exposed to vapors of 1000 and 4500 ppm of the mixture for 6 h/d, 5 d/wk, for 13 wk.

An interim sacrifice was conducted after 28 d. There were mild, transient kidney effects noted in male rats at this time. At the termination of the study there was no evidence of hydrocarbon-induced nephropathy in either sex. Therefore, the rats were judged not to be significantly affected by the exposures (Aranyi et al., 1986).

TABLE 2. Short-Term Inhalation Studies in Animals

Species	Concentration	Study/duration	Effects/references
Rat, Sprague-Dawley, albino	Isobutane (A-31 hydrocarbon) propellant/ nominal conc. 32.21 mg/L (actual 13,023 ppm)	Acute 4-h LC50 inhalation exposure to vapors, 14 d observation	Acute LC50 4-h inhalation > 13,023 ppm; no deaths; no gross signs or symptoms of intoxication; all animals appeared normal throughout entire study; reductions in body weights in males 2 and 3 d postexposure and in females throughout exposure period; necropsy: gross observations not related to test material (Phillips Petroleum Co., 1982)
Mouse	52%[a] 36% 65%	LC50/2 h	LC50 (2 h) = 52% no deaths 100% mortality (Aviado et al., 1977).
Mouse, SPF (CD-1, COBS), males	Nominal: 32.21 mg/L (actual conc. 12,460 ppm)	Respiratory tract irritancy, head only exposure to vaporized material; 1 min exposure, 10 min air; 1 min exposure, 5 min air	No patterns of respiratory pauses; exposure to isobutane at a conc. of 12,640 ppm by inhalation failed to produce respiratory irritancy in mice (Phillips Petroleum Co., 1982)
Mouse	15% 23% 35% 41% 52%	60 min 26 min 25 min 3 min 2 h 2 min 2 h	Excitement, light anesthesia Excitement, light anesthesia Anesthetic (loss of posture) Loss of posture 60% Deaths; among survivors—quick recovery (avg. 3–4 min) and normal 2 h after anesthesia Loss of posture 100% Deaths (Stoughton & Lamson, 1936)
Dog	45% 55%	10 min/tracheal cannula	Anesthetic Lethal Extremely difficult to produce good anesthesia and relaxation with any of test materials, in contrast with cyclopropane (Stoughton & Lamson, 1936)

TABLE 2. Short-Term Inhalation Studies in Animals (*Continued*)

Species	Concentration	Study/duration	Effects/references
Rabbit, New Zealand albino	22% Isobutane in a hair setting spray	Acute inhalation toxicity: 10 aerosol bursts at 13.2 g/ 30-s burst (2.9 g isobutane/burst) in a 0.34 m^3 chamber (calculated as 3575 ppm/burst or 35,750 ppm/ 10 bursts)	No deaths, abnormal behavior, changes in body weight either during exposure or after 14-d observation; no changes attributed to inhalation in gross and microscopic exams; respiratory tissues similar to untreated controls (CTFA, 1979)
Rat, Sprague-Dawley	Various conc. up to 4437 ppm of a 25% w/w blend of isobutane, *n*-butane, *n*-pentane, and isopentane	3 wk, 6 h/d, 5 d/wk	No clinical signs of distress; no evidence of kidney lesions; hematology and clinical chemistry within norm (Halder et al., 1986)

*Balanced with oxygen to prevent asphyxia.

Subchronic inhalation of isobutane as an ingredient in cosmetic preparations produced no toxicity in two different species, rabbits and monkeys (Table 3). There were no adverse effects in New Zealand albino rabbits exposed to a hairspray aerosol containing 22% isobutane sprayed twice daily, 5 d/wk for 90 d, 11.5 g/30-s aerosol spray. There were no changes in body weight, hematology, blood chemistry, and urine analysis. There was no gross or microscopic pathology, and there were no deaths (CTFA, 1979). There was no toxicity in cynomolgus monkeys exposed for 90 d to an aerosol hair spray formulation containing isobutane in concentrations up to 4000 ppm (CFTA, 1979). In stumptailed monkeys (*Macaca arctoides* strain) exposed by the same regimen for 90 d to 0.5 mg/L or 5.0 mg/L of an aerosol spray deodorant containing a 21.5% methylene chloride, 64.5 wt% mixture of isobutane and propane, and 14% other components, there were no deaths, no changes in behavior, body weight, hematology, biochemistry, or urinalysis. Electrocardiograms and tidal volume rates showed no significant changes. Gross and microscopic examinations showed no abnormalities. The high concentration test group animals had observable lens nuclear outline (Meltzer et al., 1977).

Chronic Toxicity, Carcinogenicity, and Reproductive Toxicity

No chronic studies evaluating the carcinogenicity or reproductive effects of isobutane have been performed in animals. Isobutane is flammable and its vapors can be explosive. Due to low toxicity, concentrations needed in such studies would exceed the lower explosive limit.

TABLE 3. Subchronic Inhalation Studies in Animals

Species	Concentration (ppm)	Study/duration	Effects/references
Rat, F344 male and female	1000[a] or 4500[a]	13 wk, 6 h/d, 5 d/wk	No significant effects due to exposure; no evidence of hydrocarbon-induced nephropathy in either sex at end of study; however, at 28-d interim sacrifice period mild, transient kidney effects in male rats (Aranyi et al., 1986)
Rabbit, New Zealand albino	Hairspray containing 22% isobutane as an aerosol propellant	11.5 g/30-s aerosol spray; twice daily; 5 d/wk for 90 d	No changes in body weight, hematology, blood chemistry, urine analysis; no gross or microscopic pathology, and no deaths (CTFA, 1979)
Monkey, stumptailed (*Macaca arctoides*)	Deodorant with 21.5% methylene chloride, 64.5% mixture of isobutane and propane, and 14% other components 0.5 mg/L 5.0 mg/L	6 h/d, 5 d/wk for 13 wk	No deaths; no changes in behavior, body weight, hematology, biochemistry, urinalysis; electrocardiograms and tidal vol. rates showed no significant changes; gross and microscopic exams showed no abnormalities; in high-dose group, all animals had observable lens nuclear outline (Meltzer et al., 1977)
Monkey, cynomolgus	Aerosol hair spray formulation containing isobutane up to 4000 ppm	90 d	No toxicity (CTFA, 1979)

[a]For 50:50 wt% mixture of isobutane:isopentane.

Mutagenicity

Isobutane was not mutagenic in the Ames assay in *Salmonella typhimurium* strains of bacteria exposed to various concentrations of isobutane with and without metabolic activation (Kirwin et al., 1980) (Table 4).

Cardiotoxicity

The term *cardiotoxicity* refers to the potential hazard to interfere with cardiac rhythm and myocardial contraction, which may lead to tachycar-

dia (rapid heart beat), arrhythmias (irregular heart beats), ventricular fibrillation, and cardiac arrest.

The term *cardiac sensitization* refers to a chemical's potential to sensitize the heart to epinephrine-induced arrhythmias. Another way of defining cardiac sensitization is a chemical's potentiation of epinephrine-induced cardiac arrhythmias.

The term *hemodynamic effects* refers to cardiovascular pharmacologic changes such as myocardial contractility, aortic pressure, stroke volume and work, cardiac output, pulmonary vascular resistance, and, generally, the circulation of blood.

Earlier interest in using isobutane as an anesthetic, and more recently as safe propellents for aerosol medications for asthmatics and concern about solvent abuse have led to investigative studies to learn what influence industrial substances and solvents, including isobutane, have on the heart and the respiratory and circulatory systems. The potential for isobutane to affect the heart has been studied in the monkey, dog, rat, and mouse (Table 5). Some studies were done with isobutane alone. Other studies involved intravenous (iv) injections of epinephrine during the course of isobutane inhalation. Epinephrine is believed to play a role in sensitization of the heart to light petroleum hydrocarbons, both halogenated and unhalogenated. The experiments involved open chest procedures, administration of isobutane directly into the trachea of the animal, direct inhalation of isobutane in testing chambers, or inhalation of isobutane through face masks.

Summary In animal studies, inhalation of isobutane has weak cardiotoxic effects on the heart at massive concentrations of from 3-fold to 11-fold higher than its lower explosive limit (LEL) of 18,000 ppm (1.8%). The differences in potency depend on the animal species used and whether intravenous (iv) injections of epinephrine were used in the experiments. Epinephrine heightens the response so that effects on the heart occur to a greater degree and at a lower concentration of isobutane, as well as with other solvents. Isobutane administered directly into the trachea had weak cardiotoxic effects on the heart in the monkey at 100,000 ppm (no epinephrine). Isobutane did not cause cardiotoxicity in the mouse at 600,000 ppm when no epinephrine was used. These levels are respectively 5-fold, 11-fold, and 33-fold higher than isobutane's explosive limit. Isobutane sensitized the heart to iv-injected epinephrine at 200,000 ppm in the

TABLE 4. Mutagenicity Studies

Test system	Concentration	Study type/duration	Effects/reference
Salmonella typhimurium	Various	Ames test with and without metabolic activation	Not mutagenic (Kirwin et al., 1980)

TABLE 5. Cardiotoxicity and Hemodynamic Studies in Animals

Species	Concentration	Study/duration	Effects/references
Mouse, Swiss, male	60%	6 min	Isobutane alone did not induce heart arrhythmias (Aviado et al., 1997)
	20%	2 min after inhalation, injection with 6 µg/kg epinephrine hydrochloride	Arrhythmia—heart sensitized to epinephrine (Aviado & Belej, 1974)
Rat, Mendel-Osborne, male		Study of respiratory, bronchopulmonary effects; ip anesthesia,[a] tracheal tube, EKG, plethysmograph	Decreased pulmonary compliance and tidal volume, increased pulmonary resistance, slowed respiratory rate
	27%	8.7 min	Apnea
		15 min	Cardiac arrest (Friedman et al., 1973)
Dog	15 to 90%, which is between 150,000 and 900,000 ppm (mixed with oxygen)	10 min	Sensitized myocardium to epinephrine in 2/2 dogs subsequent to iv injection of epinephrine; induced ventricular fibrillation (Krantz et al., 1948)
Dog	2.5%	5 min Exposure prior to challenge iv injection of 0.008 mg/kg epinephrine	0/12 (0%), no marked responses[b];
	5.0%		4/12 (33.3%) marked responses[b] with 1 ventricular fibrillation and cardiac arrest included in marked response
	10–20%		6/6 (100%) marked responses[b] with 3 ventricular fibrillation and cardiac arrest included in marked response; weak cardiac sensitizer (Reinhardt et al., 1971)
Dog, mongrel	2.5%	Tracheal cannula in dogs anesthetized with morphine sulfate sc and chloralose iv, 5 min	Decreased pulmonary compliance
	5%		Depressed respiratory min volume
	10%[b]		No reduction in mean blood pressure, increased pulmonary resistance, low potential for tachycardia—tachycardia not statistically significant (Belej & Aviado, 1975)

TABLE 5. Cardiotoxicity and Hemodynamic Studies in Animals (*Continued*)

Species	Concentration	Study/duration	Effects/references
Dog	Up to 1.0%	Hemodynamic studies in open-chest preparation, 5 min	No reduction in any parameters, no significant changes, no reduction in cardiac output
	2.5%		Decreased myocardial contractility, pulmonary arterial flow, stroke volume, stroke work; 5.3% decrease in cardiac output
	10%		Further decrease in cardiac output and significant increase of 16.6% in pulmonary vascular resistance (Aviado et al., 1977)
Monkey, rhesus (*Macaca mulatta*)	5%	Tracheal cannula in monkeys anesthetized with sodium pentobarbital; open chest procedure; epinephrine not used; 5 min	No changes in heart rate, myocardial force, aortic blood pressure, left atrial pressure, pulmonary/arterial pressure
	10%		Arrhythmia, myocardial depression, slight tachycardia not statistically significant; drop in aortic blood pressure statistically significant; no changes in left atrial pressure or pulmonary/arterial pressure (Belej et al., 1974)
Monkey, rhesus (*Macaca mulatta*)	5%	Monkeys anesthetized with sodium pentobarbital; tracheal cannula, open chest procedure; epinephrine not used; 5 min	No influence on circulation; no changes in heart rate, pulmonary compliance, aortic blood pressure, pulmonary resistance or respiratory min volume
	10%		No influence on circulation; no changes in heart rate, pulmonary compliance; slight increase in pulmonary resistance not statistically significant; slight depressed respiratory min volume not statistically significant (Aviado & Smith, 1975)

[a]Diphenylbarbituric acid, urethane in polyethylene glycol.

[b]"Marked response," arrhythmia considered to pose serious threat to life (multiple consecutive ventricular beats) or that ended in cardiac arrest (ventricular fibrillation).

[c]Balanced with oxygen to prevent asphyxia.

mouse. Epinephrine injected intravenously into dogs during the course of isobutane inhalation induced cardiac sensitization at 50,000 ppm which is almost 3-fold higher than the explosive limit of isobutane. Inhalation of isobutane induced various hemodynamic pharmacologic effects at 2.5% (25,000 ppm) and higher.

Details of the Experimental Studies

Mice Inhalation of 60% isobutane for 6 min did not induce heart arrhythmias (irregular heart beats) in male Swiss mice. Injection of 6 μg/kg epinephrine hydrochloride following 2 min of inhalation of 20% isobutane induced arrhythmias in the mice. The investigator concluded that isobutane sensitized the heart to epinephrine-induced arrhythmia (Aviado et al., 1977; Aviado & Belej, 1974).

Rat Friedman et al. (1973) studied respiratory and bronchopulmonary effects of isobutane and six chlorofluorohydrocarbons in rats anesthetized with diphenylbarbituric acid and urethane in polyethylene glycol. Friedman et al. reported apnea and cardiac arrest after inhalation of 270,000 ppm isobutane for 8.7 min and 15 min, respectively. They reported that isobutane decreased pulmonary compliance and tidal volume.

Dog Early investigators demonstrated that anesthesia with cyclopropane caused arrhythmias to occur in the dog's heart following intravenous injection of epinephrine. Krantz et al. (1948) extended these cardiac sensitization studies in the dog to isobutane. Intravenous injection with epinephrine following 10 min of inhalation of 15 to 90% (150,000 to 900,000 ppm) isobutane mixed with oxygen induced ventricular fibrillation in 2/2 anesthetized dogs. Krantz et al. concluded that isobutane was not a satisfactory anesthetic agent in the dog.

Reinhardt et al. (1971) studied isobutane, benzene, and a series of chlorinated and fluorinated hydrocarbons for cardiac sensitization to epinephrine in dogs. Injection with a challenge dose of 0.008 mg/kg epinephrine following a 5-min inhalation of 2.5% (25,000 ppm) isobutane induced no marked responses by the heart (0/12 dogs). At 5.0% (50,000 ppm) isobutane, the same experimental procedure induced a marked response (4/12 dogs) including 1 ventricular fibrillation and cardiac arrest. At 10–20% (100,000–200,000 ppm) concentration of isobutane, epinephrine-injected dogs all developed marked responses (6/6 dogs) including 3 ventricular fibrillations and cardiac arrest (Reinhardt et al., 1971). Reinhardt et al. characterized isobutane as a weak cardiac sensitizer.

High concentrations of isobutane showed a low potential for tachycardia (rapid heart beats) in inhalation experiments in anesthetized dogs (Belej & Aviado, 1975). Both Belej and Aviado (1975) and Aviado et al. (1977) also studied hemodynamic effects of isobutane in anesthetized dogs. Inhalation through a tracheal cannula for 5 min induced decreased pulmonary compliance at 2.5% (25,000 ppm), depressed respiratory minute volume at 5% (50,000 ppm), and increased pulmonary resistance with no reduction in blood pressure at 10% (100,000 ppm) (Belej &

Aviado, 1975). There were no hemodynamic effects, no reduction in cardiac output, and no reduction in any parameters at 1.0% (10,000 ppm) tracheal inhalation of isobutane for 5 min in anesthetized dogs in an open-chest preparation (Aviado et al., 1977). At 2.5% (25,000 ppm) there was decreased myocardial contractility, pulmonary arterial flow, stroke volume, stroke work, and decreased cardiac output at 5.3% (53,000 ppm). At 10% (100,000 ppm), there was a significant increase of 16.6% in pulmonary vascular resistance (Aviado et al., 1977).

Monkey Aviado and Smith (1975) and Belej et al. (1974) studied the respiratory and circulatory systems, and cardiotoxicity in the monkey. Anesthetized rhesus monkeys inhaled 5–10% isobutane for 5 min through a tracheal cannula. No exogenous epinephrine was used. Their studies showed that there was no influence at 5% isobutane concentration on circulation, no changes in heart rate, pulmonary compliance, aortic blood pressure, pulmonary resistance, or respiratory minute volume. The Aviado study showed that at a 10% isobutane concentration there was a slight, but not statistically significant, increase in pulmonary resistance and in depressed respiratory minute volume. In an open chest procedure in the Belej et al. study at 10% isobutane there was arrhythmia, myocardial depression, a drop in aortic blood pressure, and slight tachycardia that was not statistically significant.

Conclusion Inhalation of isobutane has a weak cardiotoxic effect on the heart in animals at massive concentrations far exceeding its explosive limit. Isobutane has a weaker or less effect on the heart than does, for example, benzene and some of the chlorofluorohydrocarbons (CFCs). The most potent compounds that sensitize the heart to epinephrine-induced arrhythmias are some, but not all, of the halogenated hydrocarbons (Reinhardt et al., 1971). The compounds containing chlorine atoms produced the greatest degree of sensitization of the heart to epinephrine and compounds containing fluorine were among the weak sensitizers (Reinhardt et al., 1971). Isobutane, cyclopentane, isopentane, and 2,2-dimethylbutane were weak cardiac sensitizers to epinephrine-induced arrhythmias (Krantz et al., 1948; Expert Panel, 1982).

Absorption and Metabolism

The absorption, distribution, metabolism, storage, and excretion of a chemical are important in understanding the effects a chemical has in the body (Table 6). Isobutane can be absorbed through the lungs. Blood levels of 20–90 ng/ml isobutane have been detected in human volunteers exposed to 500 ppm (Stewart et al., 1977). Wagner (1974) reported that 14% isobutane was absorbed in volunteer subjects inhaling 100 ppm isobutane for 20 min. Studies were done on the pulmonary absorption of inhaled vapors of 20 individual gasoline-related hydrocarbon vapors, including isobutane (API, 1987). Male F344 rats were exposed to 1000–5000 ppm isobutane vapors for 80 to 100 min. The uptake for isobutane

TABLE 6. Absorption and Metabolism Studies

Species	Concentration/route	Study type/duration	Effects/references
Volunteer subjects	100 ppm, inhalation	20 min	14% Absorbed (Wagner, 1974)
Rat, F344, males	1000–5000 ppm inhalation	Absorption studies—pulmonary absorption of 20 inhaled gasoline-related hydrocarbons—% of inhaled hydrocarbon retained; 80–100 min	5.4% Pulmonary uptake of isobutane (API, 1987)
Rat liver microsome culture in vitro study		Metabolism	Hydroxylation primarily at tertiary carbon atom, yielding 95–99% *tert*-butanol (2-methyl-2-propanol) as predominant metabolite (Frommer et al., 1970)
Mouse, male ICR	Isobutane[a] mixed with oxygen, inhalation	Metabolism study, 1-h exposure	*tert*-Butanol metabolite; isobutane found in blood, organs of animals
Mouse liver microsomes	In vitro	Metabolism study, culture	*tert*-Butanol metabolite (Tsukamoto et al., 1985)

[a]99.9% Purity isobutane.

was 5.4%. Highly volatile and branched hydrocarbons were not absorbed as well as less volatile and unbranched hydrocarbons; unsaturated compounds were better absorbed than saturated ones. Less absorption could be the reason for the reduced toxicity seen with increased branching. Although the distribution of isobutane in tissues has not been studied, distribution and absorption of isobutane in tissues such as adipose, brain, liver, and lungs can be expected (Low et al., 1987).

Low et al. (1987) stated that since isobutane is primarily eliminated unchanged in the expired air, biotransformation to water-soluble metabolites probably represents a minor route of elimination. Oxidative metabolism studies of isobutane in rat liver microsome cultures have found that hydroxylation occurs primarily at the tertiary carbon atom, yielding 95–99% tertiary butanol (2-methyl-2-propanol) as the predominant metabolite (Frommer et al., 1970). No primary alcohol (isobutanol or 2-methyl-1-propanol) was detected in this study. *tert*-Butanol cannot be oxidized to a ketone product, and therefore it is either conjugated with glucuronic acid or excreted unchanged in the expired air or urine (Low et al., 1987). More recently, Tsukamoto et al. (1985) demonstrated that isobutane is metabolized to *tert*-butanol both in vivo in ICR male mice inhaling isobu-

tane for 1 h, and in vitro by mice liver microsomes. The in vivo study involved exposure to 99.9% pure isobutane mixed with oxygen.

Human Studies

Eight female and male volunteers inhaling up to 1000 ppm isobutane for 8 h, and in repeated exposures, inhaling 500 ppm isobutane for 1, 2, or 8 h/d, 5 d/wk for 2 wk, showed no abnormalities even though isobutane was readily detected in breath and blood (Stewart et al., 1977, 1978) (Table 7). These studies reported no deviations in electrocardiograph (EKG), cardiac function or alteration in cardiac rhythm, no cardiac arrhyth-

TABLE 7. Human Studies

Population	Conc./route	Study/duration	Effects/references
Number of volunteers not specified	45 mg/m^3, inhalation	Odor recognition	Odor is recognized at 45 mg/m^3 (18.92 ppm) (Ruth, 1986)
8 male and female volunteers		Purpose: monitoring physiological responses to series of gas concentrations	No adverse effects; no ill health symptoms—no nausea, headache, eye, nose or throat irritation; all laboratory tests normal: blood count, urine and blood chemistry, alkaline-phosphatase, SGOT,
	250 ppm to 1000 ppm/inhalation	1 min 2 min 10 min 1 h 2 h 8 h	LDH, bilirubin, blood sugar, calcium and phos. levels; no deviations in neurological responses, e.g., moderate Romberg and heel to toe tests, EKG; no decrement in pulmonary or cardiac function or alteration in cardiac rhythm, no deviations in adrenocortical function, subjective responses,
	500 ppm/inhalation	1 h/d, 5 d/wk, 2 wk 2 h/d, 5 d/wk, 2 wk 8 h/d, 5 d/wk, 2 wk	cognitive response; no abnormalities even though isobutane was readily detectable in breath and blood; at end of second week
	Two mixtures of isobutane and propane/ inhalation	1 h/d, 2 d 2 h/d, 2 d 8 h/d, 2 d	of repetitive exposure, reduction in wave amplitude in the visual evoked response (Stewart et al., 1977, 1978)

(Table continues on next page)

TABLE 7. Human Studies (*Continued*)

Population	Conc./route	Study/duration	Effects/references
Case report—2-yr-old female patient	Playing with aerosol cans of deodorant, cosmetics, and shampoo; aerosol deodorant contained butane, isobutane, propane propellants, and 0.125% *tert*-butyl alcohol, zinc phenolsulfonate, propylene glycol, fragrance, benzthoniun chloride	Duration unknown	Ventricular tachycardia and seizures; patient treated with drugs and cardioversion; condition resolved after 48-h; *n*-butane, isobutane, acetone detected in serum and acetone in urine (Wason et al., 1986)
75 Volunteers, 18 to 60 yr old	Deodorant with 21.5% methylene chloride, 64.5 % mix. of isobutane and propane, and 14% other components/skin	Skin irritation study, twice daily for 12 wk	Very slight, transient erythema; reactions considered negligible
50 Volunteers 18 to 60 yr old	Antiperspirant with 20% methylene chloride, 70% mix. of isobutane and propane, and 10% other components/skin	Skin irritation study/ twice daily for 12 wk	Very slight, transient erythema; reactions considered negligible (Meltzer et al., 1977)

mia, no decrements in pulmonary function or in adrenocortical function, urine and blood chemistry, neurological response, cognitive responses, or subjective responses, and no nausea, headache, eye, or nose irritation. At the end of the second week of repetitive exposures to 500 ppm, there was a reduction in wave amplitude in the visual evoked response, possibly due to central nervous system (CNS) depression. The investigators considered the significance of this finding to be uncertain, but meriting further investigation.

Ventricular tachycardia and seizures were reported to have occurred in a 2-yr-old female patient who was playing with aerosol cans of deodorant, cosmetics, and shampoo. The aerosol deodorant contained butane, isobutane, and propane propellants, along with 0.125% *tert*-butyl alcohol, zinc phenolsulfonate, propylene glycol, fragrance, and benzthonium chloride. The patient was treated with drugs and cardioversion. The

tachycardia and seizures resolved after 48 h. *n*-Butane, isobutane, and acetone were detected in the patient's blood serum, and acetone in the urine (Wason et al., 1986).

SUMMARY

Table 8 summarizes the chemical and physical properties of isobutane.

Isobutane vapor is practically nontoxic when inhaled. Isobutane's anesthetic activity was tested in dogs (Stoughton & Lamson, 1936). At 45% (450,000 ppm), isobutane produced anesthesia in 10 min, and at 55% (550,000 ppm) it was lethal. Stoughton et al. observed that branched isomers of the saturated hydrocarbons butane and pentane showed less activity than the straight-chain compounds.

Isobutane did not produce upper airway irritancy in mice. Kidney damage did not occur in male rats breathing mixtures containing isobutane for extended periods of time.

A 12-wk twice-daily exposure to a propane–isobutane mixture present at 64.5% and 70% in two different cosmetic formulations caused transient, negligible skin irritation in 125 human volunteers.

No significant systemic abnormalities occurred in human subjects during acute inhalation studies of isobutane at exposures of 1000 ppm for 8 h/d, and at 500 ppm for 8 h/d, 5 d/wk for 2 wk.

TABLE 8. Chemical and Physical Properties of Isobutane

Description	Colorless gas with slight natural gas odor
Molecular weight	58.12
Boiling point	-11.73°C
Freezing point	-159.42°C
	-159.6°C[a]
Flashpoint	-82.7°C
	-82.78°C
Density	0.549 (20/4°C)
Density	0.5572 (20/4°C)[a]
Specific gravity	0.5631 (25°C)[a]
Vapor pressure	2 mm Hg (7.5°C) at atmospheric pressure[a]
Conversion factors	1 ppm = 2.38 mg/m^3
	1 mg/L = 420 ppm
Autoignition point	462.2°C
Explosive limit in air (LEL–UEL)[b]	1.8 to 8.4% (18,000–84,000 ppm)
Solubility	Soluble in water, very soluble in alcohol, ether, and chloroform
Reactivity	Characteristically inert
Odor recognition	45 mg/m^3 or 19 ppm (Ruth, 1986)

Note. From Expert Panel (1982).

[a]Cavender (1994).

[b]LEL–UEL, lower explosive limit to upper explosive limit.