383-94 (1995) (3) Doskey PV et al; J Air Waste Manage Assoc 42: 1437-45 (1992)]

HUMAN EXPOSURE

Probable Routes of Human Exposure:

1. Longterm personal samples for isobutane obtained at a high volume service station in eastern Pennsylvannia (n=18) resulted in the following distribution profile (number, concn): 1, not detected; 14, <0.1 ppm; and 3, 0.1-0.3 ppm(1). Air exposures were obtained for 55 components of gasoline measured by 8 petroleum companies for service stations attendants (n=49), transport drivers (n=49), and outside operators (n=56) during the summer of 1984(2). The results for isobutane were (job category, mean concn (standard deviation), percent positive): outside operator, 0.817 (1.523) mg/cu m, 75%; transport drivers, 2.867 (3.438) mg/cu m, 100%; service attendant, 8.811 (9.587) mg/cu m, 100%). Isobutane respectively constituted 4.3, 6.3 and 12.6% of the total hydrocarbon exposure for these three work groups. Exposure of service station attendants was significantly reduced when vapor recovery systems were present(2). [Peer reviewed] [(1) Kearney CA, Dunham DB; Am Ind Hyg Assoc J 47: 535-9 (1986) (2) Rappaport SM et al; Appl Ind Hyg 2: 148-54 (1987)]
2. The general population is exposed to isobutane in ambient air, especially in areas of high traffic and service stations as well as by dermal contact with petroleum products. Inhalation exposure and dermal contact may also result when using consumer products such as insect sprays, window and glass cleaners, personal spray deodorants, and rug and upholstery cleaners that contain isobutane. Occupation exposure will be by inhalation and dermal contact related to the use of fuel products and inhalation of engine exhaust.(SRC) [Peer reviewed]
3. NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,0006,228 workers are potentially exposed to isobutane in the USA(1). Ninety-eight percent of the exposures are to trade name compounds containing isobutane. [Peer reviewed] [(1) NIOSH; National Occupational Exposure Survey (1989)]

Average Daily Intake:

AIR INTAKE (assume median concn 1.26 ppb(1)): 0.61 mg; FOOD INTAKE: insufficient data; WATER INTAKE: insufficient data (SRC). [Peer reviewed] [(1) Hendler AH, Crow WL; In: Proc Annu Meet Air Waste Manage Assoc, 85th (Vol 2B), 92/75.05 (1992)]

Body Burdens:

Isobutane was not identified in any of the 12 samples of breath analyzed in Bayonne and Elizabeth, NJ as part of the USEPA Total Exposure Assessment Methodology (TEAM) study(1). [Peer reviewed] [(1) Wallace LA; Toxicol Environ Chem 12: 215-36 (1986)]

8.0 EXPOSURE STANDARDS AND REGULATIONS

OCCUPATIONAL PERMISSIBLE LEVELS

NIOSH Recommendations: Recommended Exposure Limit: 10 Hr Time-Weighted Avg: 800 ppm (1900 mg/cu m). [QC reviewed] [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997., p. 176]

9.0 MONITORING AND ANALYSIS METHODS

Analytical Laboratory Methods:

1. GAS CHROMATOGRAPHIC METHOD FOR IDENTIFICATION OF PROPELLANTS & AERATING AGENTS IN AEROSOL WHIPPED TOPPINGS & ANTISTICK PAN COATINGS. [Peer reviewed] [PAGE BD; J ASSOC OFF ANAL CHEM 61 (4): 989-92 (1978)]
2. ADVANTAGES & LIMITATIONS OF GAS CHROMATOGRAPHIC SEPARATION COLUMN IN ANALYSIS OF HYDROCARBON EMISSIONS ARE DISCUSSED. [Peer reviewed] [SCHNEIDER W, FROHNE JC, BRUDERRECK H; J CHROMATOGR 155 (2): 311-27 (1978)]

I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 75-28-5
CAS No.	75-28-5
EINECS Name	isobutane
EINECS No.	200-857-2
Molecular Formula	C4H10

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

Creation date:	19-FEB-2000
Number of Pages:	47
Chapters:	all
Edition:	Year 2000 CD-ROM edition
Flags:	non-confidential

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

-

5.1.2 Acute Inhalation Toxicity

Type:	LC50
Species:	rat
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	15 minute(s)
Value:	= 570000 ppm
Method:	other: no data
Year:	1982 **GLP:** no data
Test substance:	no data
Source:	REPSOL PETROLEO,S.A. MADRID

(38)

Type:	LC50
Species:	rat
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	15 minute(s)
Value:	> 800000 ppm
Method:	other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year:	1982 **GLP:** no data
Test substance:	other TS
Remark:	Groups of 6 male or 6 female specific pathogen-free (SPS) Alderley Park rats were exposed to various concentrations of propane in air for 15 minutes. Where deaths occurred, they were during, not after, exposure and were associated with depressant effects on the central nervous system (CNS). Recovery from non-lethal exposure was rapid, and affected animals appeared normal within 10 minutes.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	Propane, CAS No. 74-98-6

(39)

Type:	LC50
Species:	rat
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	15 minute(s)
Value:	570000 ppm
Method:	other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year:	1982 **GLP:** no data
Test substance:	other TS
Remark:	Groups of 6 male or 6 female specific pathogen-free (SPS) Alderley Park rats were exposed to various concentrations of isobutane in air for 15 minutes. Where deaths occurred, they were during, not after, exposure and were associated with stimulant effects on the central nervous system (CNS). Recovery from non-lethal exposure was rapid, and affected animals appeared normal within 10 minutes.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	Isobutane, CAS No. 75-28-5

(39)

Type:	LC50
Species:	rat
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	4 hour(s)
Value:	658 mg/l
Method:	other: procedure as detailed in paper by Shugaev (see Reference).
Year:	1969 **GLP:** no data
Test substance:	other TS
Remark:	Rats were exposed to a range of butane concentrations in air for 4 hours. Following exposure, hydrocarbon accumulation in several organs was determined. n-Butane is partially absorbed by rat tissue and partly transfered to brain, kidney, liver and perinephric adipose tissue.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	n-Butane, CAS No. 106-97-8

(40)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 15 minute(s)
Value: = 570000 ppm
Method: other: no data
Year: **GLP:** no data
Test substance: no data
Remark: Rats of the Alderley Park strain (6 male or female animals) were exposed to isobutane in various concentrations.
Range of LC50: 48 - 65 % v/v.
57 % v/v = 570000 ppm = 1375 g/l.
Source: Huels AG Marl

(41)

Type: other: EC50(CNS)
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value: 280000 ppm
Method: other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year: 1982 **GLP:** no data
Test substance: other TS
Remark: EC50(CNS) is the effective concentration causing either stimulation or depression of the central nervous system (CNS) in half the animals tested.
Groups of 6 male or 6 female specific pathogen-free (SPS) Alderley Park rats were exposed to various concentrations of propane in air for 10 minutes. Where deaths occurred, they were during, not after, exposure and were associated with depressant effects on the central nervous system (CNS). Recovery from non-lethal exposure was rapid, and affected animals appeared normal within 10 minutes.
Source: Phillips Petroleum Company Norway Tananger
Test substance: Propane, CAS No. 74-98-6

(39)

Type: other: EC50(CNS)
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value: 200000 ppm
Method: other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year: 1982 **GLP:** no data
Test substance: other TS
Remark: EC50(CNS) is the effective concentration causing either

stimulation or depression of the central nervous system (CNS) in half the animals tested.
Groups of 6 male or 6 female specific pathogen-free (SPS) Alderley Park rats were exposed to various concentrations of isobutane in air for 10 minutes. Where deaths occurred, they were during, not after, exposure and were associated with stimulant effects on the central nervous system (CNS). Recovery from non-lethal exposure was rapid, and affected animals appeared normal within 10 minutes.

Source: Phillips Petroleum Company Norway Tananger
Test substance: Isobutane, CAS No. 75-28-5

(39)

Type: other: pulmonary compliance
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other: procedure as detailed in paper by Friedman, Cammarato and Aviado (see Reference).
Year: 1973 **GLP:** no data
Test substance: other TS
Remark: Isobutane produced a decrease in pulmonary compliance and in the tidal volume of the rat.
Source: Phillips Petroleum Company Norway Tananger
Test substance: Isobutane, CAS No. 75-28-5

(42)

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 hour(s)
Value: 680 mg/l
Method: other: procedure as detailed in paper by Shugaev (see Reference).
Year: 1969 **GLP:** no data
Test substance: other TS
Remark: Mice were exposed to a range of butane concentrations in air for 2 hours. Following exposure, hydrocarbon accumulation in the animals' brains was determined.

The n-butane concentration found in mouse brain was very close to that found in rat brain.

Source: Phillips Petroleum Company Norway Tananger
Test substance: n-Butane, CAS No. 106-97-8

(40)

Type:	LC50
Species:	mouse
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	2 hour(s)
Value:	= 520000 ppm
Method:	
Year:	**GLP:** no data
Test substance:	no data
Remark:	no further details reported;
Source:	Huels AG Marl

(43)

Type:	LCLo
Species:	mouse
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	2 hour(s)
Value:	1041 mg/l
Method:	other: no data
Year:	1936 **GLP:** no data
Test substance:	no data
Source:	REPSOL PETROLEO,S.A. MADRID

(44)

Type:	other: EC50(cardiac sensitization to adrenaline)
Species:	dog
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	5 minute(s)
Value:	180000 ppm
Method:	other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year:	1982 **GLP:** no data
Test substance:	other TS
Remark:	Dogs were exposed to hydrocarbon/air mixtures for five minutes for the determination of EC50(CS). EC50(cardiac sensitization to adrenaline) is the effective concentration causing cardiac sensitization to adrenaline in half the animals tested.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	Propane, CAS No. 74-98-6

(39)

Type: other: EC50(cardiac sensitization to adrenaline)
Species: dog
Sex:
Number of Animals:
Vehicle:
Exposure time: 5 minute(s)
Value: 70000 ppm
Method: other: procedure as detailed in paper by Clark and Tinston (see Reference).
Year: 1982 **GLP:** no data
Test substance: other TS
Remark: Dogs were exposed to hydrocarbon/air mixtures for five minutes for the determination of EC50(CS).
EC50(cardiac sensitization to adrenaline) is the effective concentration causing cardiac sensitization to adrenaline in half the animals tested.
Source: Phillips Petroleum Company Norway Tananger
Test substance: Isobutane, CAS No. 75-28-5

(39)

Type: other: cardiac sensitization to epinephrine
Species: dog
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value:
Method: other: procedure as detailed in paper by Krantz, Carr and Vitcha (see Reference).
Year: 1948 **GLP:** no data
Test substance: other TS
Remark: Test Method

Dogs in groups of 2 to 12 were exposed to individual liquid or gaseous hydrocarbons in air at concentrations of 10% to 90%, following intravenous injection with epinephrine.
Cardiac sensitization was determined from electrocardiogram recordings of anaesthetized animals.
Test Results

All hydrocarbons tested, except ethylene, caused cardiac sensitization.

None of the twelve dogs exposed to ethylene demonstrated cardiac sensitization. Two of the four dogs exposed to ethane were sensitized. Most of the dogs exposed to the other hydrocarbons were sensitized.
Source: Phillips Petroleum Company Norway Tananger
Test substance: Test Substances - test substances used were: ethane, propane, propylene, butane, isobutane, 2-butene, cyclobutane, cyclobutene, cyclopentane, isopentane and 2,2-dimethyl butane.

(45)

5.1.3 Acute Dermal Toxicity

-

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species:	rabbit
Concentration:	
Exposure:	
Exposure Time:	
Number of Animals:	
PDII:	
Result:	
EC classificat.:	
Method:	
Year:	**GLP:** no data
Test substance:	no data
Remark:	Unpublished CTFA data (CFTA, Jan. 22, 1981. Submission of data by CFTA: Data on cosmetic products) are cited. Isobutane in concentrations of 75.75 % to 89.55 % was applied to the intact shaved back skin of rabbits (15 studies with 6 animals each). No to moderate erythema and edema were produced. Primary irritation indices ranged from 0.29 to 2.025 (on a 0-8 scale). not classifiable according to current EEC directives;
Source:	Huels AG Marl

(46)

5.2.2 Eye Irritation

Species:	rabbit
Concentration:	
Dose:	
Exposure Time:	
Comment:	
Number of Animals:	
Result:	not irritating
EC classificat.:	not irritating
Method:	other: procedure as detailed in book by Grant (see Reference).
Year:	**GLP:** no data
Test substance:	other TS
Remark:	Injection of liquid butane into the anterior eye chamber of rabbits did not cause disturbance, and all effects disappeared in 2-4 days.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	n-Butane, CAS No. 106-97-8

(47)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: Unpublished CTFA data (CFTA, Aug. 9, 1979. Submission of data by CFTA: Data on cosmetic products) are cited.
A hair spray containing 22% of isobutane was tested for eye irritation in five rabbits. A 0.1 ml of the undiluted product was sprayed into one eye, and after 4 sec the eye was irrigated. There was no sign of corneal irritation after 1 hour. There was transient iritis and mild conjunctivitis after 1 hour, but these soon disappeared.
not classifiable according to current EEC directives;
Source: Huels AG Marl

(46)

5.3 Sensitization

-

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 90 days
Frequency of treatment: 6 hours per day, 5 days per week
Post. obs. period:
Doses: 2 Test groups: 1017 ppm and 4489 ppm (20 male/10 female per group). Negative control group: no treatment (40 male/20 female animals).
Control Group: yes, concurrent no treatment
NOAEL: 4489 ppm
Method: other: procedure as detailed in paper by Aranyi (see Reference).
Year: 1986 **GLP:** no data
Test substance: other TS
Remark: Atmospheric concentrations were monitored during the study. The main objective of the study was to establish the renal effects of gaseous hydrocarbons.
Result: There were NO DEATHS, and NO OTHER SIGNIFICANT TOXICOLOGICAL EFFECTS were found.

Serial sacrifices of 10 male and 5 female animals were made after 28 days. The male animals in these groups showed mild but significant effects characteristic of light

hydrocarbon nephropathy. However, at 90 days the animals showed no evidence of kidney effects.

Clinical signs included HUNCHED POSTURE, LETHARGY and INTERMITTENT TREMOR. No effects were evident from bodyweights, haematological and biochemical parameters, or from histopathology.

Source: Phillips Petroleum Company Norway Tananger
Test substance: Tests were carried out on two gas mixtures comprising:
50% n-butane and 50% n-pentane, and
50% iso-butane and 50% iso-pentane.

(48)

Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 21 days
Frequency of treatment: 6 hours per day, 5 days per week
Post. obs. period:
Doses: 3 Test groups: 0.12 mg/l, 1.15 mg/l and 11.80 mg/l (10 male/10 female per group). Negative control group: no treatment (10 male/10 female animals).
Control Group: yes, concurrent no treatment
NOAEL: 11.8 mg/l
Method: other: procedure as detailed in paper by Halder et al. (see Reference).
Year: 1986 **GLP:** no data
Test substance: other TS
Remark: Atmospheric concentrations were monitored during the study. The main objective of the study was to establish if typical C4 and C5 hydrocarbons could cause kidney damage in male rats.
Result: NO SIGNIFICANT TOXICOLOGICAL EFFECTS were found.

Animals showed no clinical signs of distress.

Haematological and biochemical parameters were not significantly different from the negative control group. Bodyweight gains were not abnormal. In particular, there was no evidence of treatment-related pathological lesions, especially the kidney lesions found in male rats exposed to unleaded gasoline vapour.

Source: Phillips Petroleum Company Norway Tananger
Test substance: Tests were carried out on a gas mixture containing 25% by weight of each of the hydrocarbon constituents n-butane, isobutane, n-pentane and isopentane.

(49)

Species:	rat **Sex:** male/female
Strain:	Fischer 344
Route of admin.:	inhalation
Exposure period:	13 weeks
Frequency of treatment:	6 hr/day, 5 days/week
Post. obs. period:	none
Doses:	0, 1000 or 4500 ppm
Control Group:	yes
Method:	other: as described by author
Year:	1984 **GLP:** yes
Test substance:	other TS: 50 :50 mixtures of isobutane:isopentane
Remark:	The inhalation toxicity of a 50:50 mixture of isobutane:isopentane was evaluated. Subgroups of the male hydrocarbon-exposed and filtered air-exposed control rats were sacrificed after 4 weeks, the remaining animals after completion of the 13-week exposure. At both the interim and terminal sacrifices a complete necropsy evaluation was performed and the kidneys preserved for histopathological evaluation.
Result:	Only minimal numbers of incidences of exposure-related toxic effects were observed throughout the study. Body weights were unaffected for rats exposed to 1000 or 4500 ppm relative to controls. Gross lesions observed at necropsies performed for subgroups of male rats after 4 exposure weeks, and for the remaining male and all female rats after completion of the 13-week period were considered to be spontaneous and unrelated to the exposures. No evidence of hydrocarbon nephropathy in male or female rats from any treatment group was observed.
Source:	Huels AG Marl

(50)

5.5 Genetic Toxicity 'in Vitro'

Type:	Ames test
System of testing:	Salmonella typhimurium, reverse mutation assay using strains TA98, TA100, TA1535, TA1537 and TA1538.
Concentration:	atmospheric concentrations of 5, 10, 20, 30, 40, and 50% (vol/vol) in air
Metabolic activation:	with and without
Result:	negative
Method:	other: OECD guideline 479 method adapted to test gaseous substances
Year:	**GLP:** no data
Test substance:	other TS
Remark:	Five strains of Salmonella typhimurium were exposed for six hours to concentrations of up to 50% (vol/vol) of propane in air. 50% was the highest non-toxic dose. There was no evidence of a significant increase in mutation frequency either in the presence or absence of metabolic activation.
Source:	Phillips Petroleum Company Norway Tananger
Test substance:	Propane, CAS No. 74-98-6

(51)

Type: Ames test
System of testing: Salmonella typhimurium, reverse mutation assay using strains TA98, TA100, TA1535, TA1537 and TA1538.
Concentration: atmospheric concentrations of 5, 10, 20, 30, 40, and 50% (vol/vol) in air
Metabolic activation: with and without
Result: negative
Method: other: OECD guideline 479 method adapted to test gaseous substances
Year: **GLP:** no data
Test substance: other TS
Remark: Five strains of Salmonella typhimurium were exposed for six hours to concentrations of up to 50% (vol/vol) of butane in air. 50% was the highest non-toxic dose. There was no evidence of a significant increase in mutation frequency either in the presence or absence of metabolic activation.
Source: Phillips Petroleum Company Norway Tananger
Test substance: n-Butane, CAS No. 106-97-8

(51)

Type: Ames test
System of testing: Salmonella typhimurium, reverse mutation assay using strains TA98, TA100, TA1535, TA1537 and TA1538.
Concentration: atmospheric concentrations of 5, 10, 20, 30, 40, and 50% (vol/vol) in air
Metabolic activation: with and without
Result: negative
Method: other: OECD guideline 479 method adapted to test gaseous substances
Year: **GLP:** no data
Test substance: other TS
Remark: Five strains of Salmonella typhimurium were exposed for six hours to concentrations of up to 50% (vol/vol) of isobutane in air. 50% was the highest non-toxic dose. There was no evidence of a significant increase in mutation frequency either in the presence or absence of metabolic activation.
Source: Phillips Petroleum Company Norway Tananger
Test substance: Isobutane, CAS No. 75-28-5

(51)

Type: Ames test
System of testing: Salmonella typhimurium TA 1535, 1537, 1538, 98, and 100
Concentration: 5, 10, 20, 30, 40, and 50 % v/v
Metabolic activation: with and without
Result: negative
Method: other: as described by author
Year: 1980 **GLP:** no data
Test substance: no data
Remark: Isobutane at concentrations of 5, 10, 20, 30, 40 and 50 % was assayed for mutagenicity in S. typhimurium strains TA 1535, 1537, 1538, 98 and 100. Bacteria were exposed to isobutane in a sealed 9 liter desiccator for a period of 6 hrs; 40-45 hrs after the end of exposure, revertants were counted. Isobutane was weakly toxic at 50 % in air.
Source: Huels AG Marl

(52)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration:
Metabolic activation: with and without
Result: negative
Method: other: no data
Year: **GLP:** no data
Test substance: no data
Source: Huels AG Marl

(53)

Type:
System of testing:
Concentration:
Metabolic activation:
Result:
Method:
Year: **GLP:**
Test substance:
Source: REPSOL PETROLEO,S.A. MADRID

(54)

5.6 Genetic Toxicity 'in Vivo'

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: **GLP:**
Test substance:
Source: REPSOL PETROLEO,S.A. MADRID

(54)

5.7 Carcinogenicity

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: No data concerning with carcinogenecity.
Source: REPSOL PETROLEO,S.A. MADRID

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance: other TS
Remark: 1,3-butadiene, a possible constituent of petroleum gases, has been shown to be carcinogenic in rodents in inhalation studies, but there is no direct evidence for its carcinogenicity in man.
Source: Phillips Petroleum Company Norway Tananger
Test substance: 1,3-butadiene

(55)

5.8 Toxicity to Reproduction

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Source: REPSOL PETROLEO,S.A. MADRID

(56)

5.9 Developmental Toxicity/Teratogenicity

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Source: REPSOL PETROLEO,S.A. MADRID

(57)

5.10 Other Relevant Information

Type: adsorption
Remark: The comparative rates of uptake of 19 hydrocarbon vapors by male F344/N rats were determined. Rats were exposed nose-only for 80 min on 5 consecutive days. Exposure concentrations were 1 ppm on Day 1, 10 ppm on Day 2, 100 ppm on Day 3, 1000 ppm on Day 4 and 5000 ppm on Day 5. For the inhalation of 100 ppm, the uptake range for isobutane was 0.6 +-0.1 nmol/kg/min/ppm, for 10 ppm it was 0.6 +-0.3 and 1.0 +-0.3, respectively.
Source: Huels AG Marl

(58)

Type: Metabolism
Remark: In male ICR mice having inhaled isobutane for 1 h, tert.-butanol was found as metabolite in blood and various organs. In vitro reactions with liver microsomes also produced tert.-butanol from isobutane.
Source: Huels AG Marl

(59)

Type: Neurotoxicity
Remark: The anesthetic property of isobutane was studied using 48 mice. At a 35 % concentration in air for 25 min, the compound was fairly effective as an anesthetic, but a 41-52 % concentration was lethal to 60-100 % of the animals.
Source: Huels AG Marl

(60)

Type: Neurotoxicity
Remark: Male albino rats were anesthetized i.p. and subjected to steadily increasing concentrations of isobutane in air. Isobutane caused decreases in both pulmonary compliance and tidal volume, and sensitized the heart to epinephrine-induced arrhythmias. Apnea occured at an isobutane concentration of 27 %.
Source: Huels AG Marl

(61)

Type: Neurotoxicity
Remark: Male Swiss mice were anesthetized i.v. and exposed to isobutane at concentrations of 10, 20 and 40 % in air. Isobutane did not induce arrhythmia, but at 20 % did sensitize the heart to epinephrine-induced arrythmia.
Source: Huels AG Marl

(62)

Type: Neurotoxicity
Remark: Rhesus monkeys (Macaca mulatta) were anesthetized by i.v. injection of sodium pentobarbital and exposed to atmospheres of 5 and 10 % isobutane. Isobutane caused arrythmia, myocardial depression, tachycardia, a fall in aortic blood pressure and a rise in left atrial pressure. It is suggested, that the hazard of exposure to aerosol propellants is increased in persons with heart disease.
Source: Huels AG Marl

(63)

Type: Neurotoxicity
Remark: Rhesus monkeys (Macaca mulatta) were anesthetized by i.v. injection of sodium pentobarbital and exposed to atmospheres of 5 and 10 % isobutane. Isobutane did not influence circulation but increased resistance and depressed respiratory minute volume.
Source: Huels AG Marl

(64)

Type: Neurotoxicity
Remark: Sensitization of the heart to arrhythmia in the anesthetized dog was investigated. The minimal effective concentration of isobutane influencing the cardiovascular system was 2 %.
Source: Huels AG Marl
(65)

Type: Neurotoxicity
Remark: Mongrel dogs were anesthetized and exposed to isobutane for 5 min. All parameters were taken at the end of the fifth minute. Isobutane, in concentrations as high as 20 % did not cause tachycardia, but did induce early respiratory depression, increased pulmonary resistance, and decreased pulmonary compliance.
Source: Huels AG Marl
(66)

Type: Neurotoxicity
Remark: Rats of the Alderley Park strain (6 male or females) were exposed to various concentrations of isobutane. The animals were observed for effects on the central nervous system, either stimulation (tremors of the limbs) or depression (ataxia and loss of righting reflex), over a 10 min exposure period. The EC50 CNS effect concentration (10 min) was calculated to be 20 vols % in air (16-23 vols % on the 95 % confidence level). The EC50 for cardiac sensitization to adrenaline in dogs after 5 min exposure was determined to be 7.0 vols % in air (4.7-10.6 vols % on the 95 % confidence level) (details not reported).
Source: Huels AG Marl
(41)

5.11 Experience with Human Exposure

Remark: Ikoma records 20 cases of sudden death in which propane and propylene were found in the blood, urine and cerebrospinal fluids of the victims.
Source: Phillips Petroleum Company Norway Tananger
(67)

Remark: Human volunteers exposed to isobutane concentrations ranging from 250 to 10000 ppm for up to eight hours, and to 500 ppm for one to eight hours per day for ten days, showed no deleterious effects.
Source: Phillips Petroleum Company Norway Tananger
(68)

Remark: During laboratory investigations of workers bottling liquefied gases (propane and butane), most of the workers complained of respiratory symptoms, e.g. dry cough and dry throat together with gastrointestinal effects. The electrocardiographic findings in some workers indicated sinus tachycardia, extrasystole and incomplete right bundle branch block.
Source: Phillips Petroleum Company Norway Tananger

(69)

Remark: Lactic acid production in workers experiencing propane "poisoning" was reported as slight.

Source: Phillips Petroleum Company Norway Tananger

(69)

Remark: Healthy adult male and female volunteers were exposed in small groups (1m/1f to 4m/4f) in a controlled environment chamber to isobutane. Single exposures to 250, 500 and 1000 ppm for periods of 1 min to 8 hrs were conducted. There were no untoward health effects: Cardiac and pulmonary responses, blood count, urinalysis, serum alk. phosphatase, serum glutamic-oxalacetic transaminase, lactate dehydrogenase, serum bilirubin, blood sugar, serum calcium, serum phosphate, blood urea nitrogen, spontaneous EEG, visual evoked response, cognitive tests and ACTH stimulation tests were unaltered.

Source: Huels AG Marl

(70)

Remark: Healthy young male and female volunteers were exposed to 500 ppm isobutane for 1, 2 or 8 hrs/day, 5 days/week, for a total of 2 weeks. Repetitive exposures to isobutane were without measurable untoward physiological effects: Cardiac and pulmonary responses, blood count, urinalysis, serum alk. phosphatase, serum glutamic-oxalacetic transaminase, lactate dehydrogenase, serum bilirubin, blood sugar, serum calcium, serum phosphate, blood urea nitrogen, spontaneous EEG, visual evoked response, cognitive tests and ACTH stimulation tests were unaltered.

Source: Huels AG Marl

(70)