NITROMETHANE

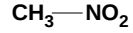
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 75-52-5
Chem. Abstr. Name: Nitromethane
IUPAC Systematic Name: Nitromethane
Synonyms: Nitrocarbol

1.1.2 *Structural and molecular formulae and relative molecular mass*



CH_3NO_2 Relative molecular mass: 61.04

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Colourless, oily liquid with a moderately strong, somewhat disagreeable odour (Budavari, 1998)
(*b*) *Boiling-point*: 101.1 °C (Lide & Milne, 1996)
(*c*) *Melting-point*: –28.5 °C (Lide & Milne, 1996)
(*d*) *Density*: 1.1371 g/cm^3 at 20 °C (Lide & Milne, 1996)
(*e*) *Spectroscopy data*: Infrared (grating [25]), Raman [296], ultraviolet [29], nuclear magnetic resonance (proton [9146], C-13[4002]) and mass spectral data have been reported (Sadtler Research Laboratories, 1980; Lide & Milne, 1996)
(*f*) *Solubility*: Slightly soluble in water (95 mL/L at 20 °C; Budavari, 1998) acetone, alkali (bases), carbon tetrachloride, diethyl ether and ethanol (Lide & Milne, 1996; Verschueren, 1996; American Conference of Governmental Industrial Hygienists, 1999)

(*g*) *Volatility*: Vapour pressure, 3.7 kPa at 20 °C; relative vapour density (air = 1), 2.11; flash-point, 35 °C (closed-cup) (Verschueren, 1996; American Conference of Governmental Industrial Hygienists, 1999)

(*h*) *Stability*: Lower explosive limit in air, 7.3% by volume; sensitive to adiabatic compression (Angus Chemical Co., 1998); forms an explosive sodium salt which bursts into flame on contact with water (Budavari, 1998)

(*i*) *Octanol/water partition coefficient (P)*: log P, –0.35 (Hansch *et al*., 1995)

(*j*) *Conversion factor*[1]: $mg/m^3 = 2.50 \times ppm$

1.1.4 *Technical products and impurities*

Nitromethane is commercially available with the following specifications (by weight): purity, 98.0% min.; total nitroparaffins, 99.0% min.; acidity (as acetic acid), 0.1% max.; and water, 0.1% max. Nitromethane can be made less sensitive to detonation by shock by the addition of compounds such as alcohols, hydrocarbons, esters and ketones. These desensitizers, with the minimum content by weight that must be present in the mixtures, are: cyclohexanone (25%), 1,4-dioxane (35%), 1,2-butylene oxide (40%), methanol (45%), 2-nitropropane (47%), 1-nitropropane (48%) or methyl chloroform (50%) (Angus Chemical Co., 1998).

1.1.5 *Analysis*

Nitromethane can be determined in workplace air by adsorbing the air sample on Chromosorb, desorbing with ethyl acetate and analysing by gas chromatography with nitrogen-specific detection (method 2527) (Eller, 1994).

1.2 Production

Nitromethane was first prepared in 1872 by Kolbe, and is produced commercially by high-temperature vapour-phase nitration of propane. The process, which uses nitric acid as the nitrating agent, is based on a free-radical reaction in which the active species is the NO_2 radical (Markofsky, 1991; Angus Chemical Co., 1998).

Information available in 1999 indicated that nitromethane was manufactured by four companies in China, two companies in India and one company each in Germany, Spain and the United States (Chemical Information Services, 1999).

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[1] Calculated from: mg/m^3 = (relative molecular mass/24.45) × ppm, assuming a temperature of 25 °C and a pressure of 101 kPa

1.3 Use

One of the most important direct uses for nitromethane is in the stabilization of halogenated hydrocarbons. For example, small amounts of nitromethane are widely used in industry to form stable non-corrosive mixtures with 1,1,1-trichloroethane for vapour degreasing, dry cleaning and for cleaning semiconductors and lenses. It is also used to stabilize the halogenated propellants for aerosols and to inhibit corrosion on the interiors of tin-plated steel cans containing water-based aerosol formulations (Markofsky, 1991; Angus Chemical Co., 1998).

Nitromethane is frequently used as a polar solvent for cellulose esters (Lundberg, 1989) and for cyanoacrylate adhesives and acrylic coatings. It is also used for cleaning electronic circuit boards. Nitromethane alone, and in mixtures with methanol and other nitroparaffins, is used as a fuel by professional drag racers and hobbyists. The explosives industry uses nitromethane in a binary explosive formulation and in shaped charges (Markofsky, 1991; Angus Chemical Co., 1998).

Nitromethane is used as a metal stabilizer for various chlorinated and fluorinated hydrocarbon solvents. The primary role of the nitromethane is to complex metal salts from the solvent–metal corrosion reaction (Archer, 1996).

1.4 Occurrence

1.4.1 *Natural occurrence*

Nitromethane is not known to occur as a natural product.

1.4.2 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1999) as many as 135 000 workers in the United States were potentially exposed to nitromethane (see General Remarks).

1.4.3 *Environmental occurrence*

The production of nitromethane and its use as a solvent, fuel additive, stabilizer for halogenated alkanes, and intermediate may result in the release of nitromethane into the environment, principally into the atmosphere. Human exposure to nitromethane may additionally occur via dermal contact and accidental ingestion of methanol–nitromethane fuel mixtures (Kaiffer *et al.*, 1972; Sandyk & Gillman, 1984; Dayal *et al.*, 1989; De Leacy *et al.*, 1989; Lundberg, 1989; National Toxicology Program, 1997; Mullins & Hammett-Stabler, 1998).

The concentration of nitromethane in automobile exhaust using nine hydrocarbon test fuels under simulated driving conditions ranged from < 0.8 to 5.0 ppm (Seizinger & Dimitriades, 1972).

Nitromethane has been found in one of twelve samples of mother's milk (Pellizzari *et al*., 1982).

1.5 Regulations and guidelines

Occupational exposure limits and guidelines for nitromethane are presented in Table 1.

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

3.1 Inhalation exposure

3.1.1 *Mouse*

Groups of 50 male and 50 female B6C3F_1 mice, seven weeks of age, were exposed by inhalation to 0, 188, 375 or 750 ppm [0, 470, 938 or 1875 mg/m^3] nitromethane (purity, 98%, with 0.25% nitroethane and 0.03% 2-nitropropane as contaminants) for 6 h plus T_{90} (12 min) per day on five days per week for 103 weeks [T_{90} is the time to achieve 90% of the target concentration]. The high dose was estimated to be the maximal tolerated dose. The average age of mice at necropsy was 111–112 weeks. The mean survival was 681, 700, 674 and 687 days among males and 662, 663, 673 and 695 days among females in the respective dose groups. As summarized in Table 2, statistically significant increases in the incidence of Harderian gland tumours and of alveolar/bronchiolar tumours in males and females and of hepatocellular adenomas in females were observed (National Toxicology Program, 1997).

3.1.2 *Rat*

Groups of 50 male and 50 female Fischer 344/N rats, seven weeks of age, were exposed by inhalation to concentrations of 0, 94, 188 or 375 ppm [0, 135, 470 or 938 mg/m^3] nitromethane (purity, 98%, with 0.25% nitroethane and 0.03% 2-nitropropane as contaminants) for 6 h plus T_{90} (12 min) per day on five days per week for 103 weeks. The high dose was estimated to be the maximal tolerated dose. The average age of rats at necropsy was 111 weeks. The mean survival was 642, 631, 646 and 640 days among males and 683, 653, 679 and 670 days among females in the respective dose groups. The incidences of mammary gland fibroadenomas were increased in females

Table 1. Occupational exposure limits and guidelines for nitromethane[a]

Country	Year	Concentration (mg/ m^3)	Interpretation[b]
Denmark	1993	250	TWA
Finland	1993	250	TWA
		375	STEL
France	1993	250	TWA
Germany	1998	250	TWA
Ireland	1997	250	TWA
		375	STEL
Netherlands	1997	50	TWA
Philippines	1993	250	TWA
Poland	1998	30	TWA
		240	STEL
Switzerland	1993	250	TWA
Turkey	1993	250	TWA
United Kingdom	1997	250	TWA
		375	STEL
United States			
ACGIH	1999	50	TWA
OSHA	1999	250	TWA

[a] From Finnish Ministry of Social Affairs and Health (1998); Occupational Safety and Health Administration (OSHA) (1999); American Conference of Governmental Industrial Hygienists (ACGIH) (1999); National Library of Medicine (1999)

[b] TWA, time-weighted average; STEL, short-term exposure limit

[c] These countries follow the recommendations of the ACGIH threshold limit values: Bulgaria, Colombia, Jordan, Republic of Korea, New Zealand, Singapore and Viet Nam

(19/50, 21/50, 33/50 ($p < 0.001$, logistic regression test), and 36/50 ($p < 0.001$, logistic regression test)), as were those of mammary gland carcinomas (2/50, 7/50, 1/50 and 11/50 ($p < 0.05$, logistic regression test)) in the control, low-, mid- and high-dose groups, respectively (National Toxicology Program, 1997).

Groups of 40 male and 40 female BLU:(LE)BR Long-Evans rats [age unspecified] were exposed by inhalation to 0, 100 or 200 ppm [0, 250 or 500 mg/m^3] nitromethane (purity, 96.26%, with 2.79% nitroethane and 0.62% 2-nitropropane as contaminants) for 7 h per day on five days per week for two years. There was no difference in body weight gain in males, but body weight gain in females exposed to 100 or 200 ppm was slightly less than that of controls. The numbers of survivors at the end of the experiment were 25, 23 and 25 (males) and 30, 29 and 24 (females) in the control, low- and high-dose

Table 2. Incidence of tumours in B6C3F$_1$ mice exposed by inhalation to nitromethane

	Number of animals with tumours			
	0 ppm	188 ppm	375 ppm	750 ppm
Males				
Harderian gland adenoma	9/50	10/50	19/50*	32/50**
Harderian gland carcinoma	1/50	1/50	6/50	5/50
Harderian gland adenoma or carcinoma	10/50	11/50	25/50**	37/50**
Alveolar/bronchiolar adenoma	11/50	10/50	9/50	12/50
Alveolar/bronchiolar carcinoma	2/50	3/50	3/50	11/50**
Alveolar/bronchiolar adenoma or carcinoma	13/50	13/50	12/50	20/50
Females				
Harderian gland adenoma	5/50	7/50	16/50**	19/50**
Harderian gland carcinoma	1/50	2/50	4/50	3/50
Harderian gland adenoma or carcinoma	6/50	9/50	20/50**	21/50**
Hepatocellular adenoma	14/50	24/49**	17/49	35/50**
Hepatocellular carcinoma	10/50	14/49	8/49	12/50
Hepatocellular adenoma or carcinoma	19/50	34/49**	22/49	40/50**
Alveolar/bronchiolar adenoma	3/50	3/50	2/49	9/50
Alveolar/bronchiolar carcinoma	0/50	3/50	5/49*	3/50
Alveolar/bronchiolar adenoma or carcinoma	3/50	6/50	6/49	12/50*

From National Toxicology Program (1997)
* $p \leq 0.05$, logistic regression test
* $p \leq 0.01$, logistic regression test

groups, respectively. There was no significant increase in the incidence of tumours related to nitromethane (Griffin *et al.*, 1996).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Nitromethane was administered to Wistar rats [sex not specified] by a single lethal intraperitoneal injection of 1.5 g/kg body weight (bw), by eight injections of 0.11 g/kg

bw over two weeks, or by inhalation of a lethal concentration of 33 g/m^3 for about 6 h. In all cases no methaemoglobin was detected in the blood and low concentrations of nitrite were found in the heart, lungs, kidney and spleen, but not in the liver. After the inhalation study nitromethane was detected only in the liver (Dequidt *et al.*, 1973).

Formaldehyde generated from nitromethane was found only in trace amounts after incubation with microsomes from from Fischer 344 rat liver, but none was found after incubation with rat nasal microsomes (Dahl & Hadley, 1983). Nitromethane inhibited rabbit liver cytochrome P450 activity, apparently competing for the same ferrohaemochrome-binding sites as carbon monoxide (Wade *et al.*, 1977).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

Nitromethane was administered intraperitoneally (200 mg/kg bw) to male Wistar rats (three months of age) as a 10% solution in olive oil. The effects of nitromethane in the liver were detected only 48 h after administration and included a decrease in NADPH-cytochrome c reductase activity with proliferation of the smooth endoplasmic reticulum. Nitromethane also caused an increase in brain acid proteinase (4 h after injection) and acetylcholine esterase activities (4, 24 and 48 h after injection) (Zitting *et al.*, 1982).

BALB/c male mice (19–25 g) received a single intraperitoneal injection of 4.5, 6.7 or 9.0 mmol/kg bw nitromethane in a volume of 0.2 mL saline. Control mice were injected with the same volume of 0.9% sodium chloride. Mice were killed 24, 48, 72 or 96 h after treatment. Blood was obtained by cardiac puncture and plasma was analysed for changes in sorbitol dehydrogenase, alanine aminotransferase and aspartate aminotransferase activity as measures of liver damage. Sections from three different liver lobes were processed and stained with haematoxylin and eosin for histopathological analysis. There were no significant changes in any of the enzymes measured or significant abnormalities in the livers of mice following nitromethane administration, demonstrating a lack of hepatotoxicity (Dayal *et al.*, 1989).

Nitromethane has been shown to produce histidinaemia in rats. Inbred weanling male Sprague-Dawley rats given subcutaneous injections of nitromethane (1.2 mol/L, 0.4 mL/100 g bw) every other day for one, three, six, 12 and 18 days. The histidine concentration in tissues increased gradually to reach a plateau after six days of treatment and after 18 days, levels were increased 4.7-fold in plasma, 2.7-fold in brain, 3.0-fold in liver and 1.7-fold in kidney (Lee & Wang, 1975). In the same strain of rats injected subcutaneously with nitromethane (1.8 mol/L, 0.8 mL/100 g bw) every day for six days, 61% of the rats had paralysis of the limbs and 15% had occasional

seizures. Liver weights and liver total protein did not change with treatment with nitromethane. Hepatic histidase activity decreased significantly in the nitromethane-treated rats compared with controls, with approximately a 3–3.5-fold corresponding increase in histidine concentration in plasma, liver and brain. No significant change in serotonin content of the various areas of the brain or in free amino acid concentration in plasma was detected. These results are consistent with nitromethane being a histidase inhibitor (Douay & Kamoun, 1980). In male Wistar rats (30 days of age), nitromethane (730 mg/kg bw) injected intraperitoneally three times over a 24-h period caused a 90% inhibition of histidase activity and higher serum histidine levels compared with controls. A consistently lower locomotor activity was observed in these histidinaemic rats compared with controls (Dutra-Filho *et al*., 1989).

Male and female Fischer 344/N rats and B6C3F_1 mice (seven weeks of age) were exposed to 0, 94, 188, 375, 750 or 1500 ppm [0, 235, 470, 938, 1875 or 3750 mg/m^3] nitromethane by inhalation for 6 h per day on five days per week over a 16-day period for a total of 12 exposure days. The mean body weight gain of male rats exposed to 1500 ppm [3750 mg/m^3] nitromethane only was slightly but significantly decreased. There was increased preening, rapid breathing, and hyperactivity early in the study and hypoactivity and loss of coordination in the hindlimbs near the end of the study in rats of both sexes. Exposure to nitromethane caused a concentration-related increase in the absolute and relative liver weights and minimal to mild degeneration of the olfactory epithelium in the nose of rats and mice. In nitromethane-exposed male and female rats, there was sciatic nerve degeneration. Concentrations of 750 or 1500 ppm [1875 or 3750 mg/m^3] nitromethane resulted in reduced myelin around sciatic axons in rats (National Toxicology Program, 1997).

Male and female Fischer 344/N rats and B6C3F_1 mice (six weeks of age) were exposed by inhalation to 0, 94, 188, 375, 750 or 1500 ppm [0, 235, 470, 938, 1875 or 3750 mg/m^3] nitromethane for 6 h per day on five days per week for 13 weeks to evaluate the cumulative toxic effects of repeated exposure to nitromethane and to determine the appropriate exposure concentrations to be used in a two-year study. Additional groups of rats were designated for clinical pathology evaluation on days 3 and 23. Neurobehavioural tests were carried out on all core study rats during week 11 of the study. Body weight and body weight gain were significantly less in male rats exposed to 1500 ppm [3750 mg/m^3] nitromethane than in the control group. Clinical findings included hindlimb paralysis in rats exposed to 750 and 1500 ppm [1875 and 3750 mg/m^3] nitromethane. Nitromethane caused exposure-related microcytic, responsive anaemia in male and female rats. Evidence that a haemolytic process occurred in exposed rats included the presence of schistocytes, Heinz bodies and spherocytes and increased mean cell haemoglobin and methaemoglobin concentration. On exposure day 23, there was a transient decrease in serum levels of triiodothyronine, and of total and free thyroxine in male and female rats exposed to nitromethane. Nitromethane exposure also caused minimal to mild hyperplasia of the bone marrow. Both rats and mice exposed to nitromethane had olfactory epithelial degeneration and

respiratory epithelial hyaline droplets. Goblet-cell hyperplasia occurred in male and female rats. Mild degeneration of the sciatic nerve and the lumbar spinal cord was also observed in male and female rats exposed to 375 ppm [938 mg/m^3] nitromethane. Forelimb and hindlimb grip strengths decreased in rats exposed to the highest concentration of nitromethane compared with controls. Both male and female mice in the 1500-ppm exposure group had minimal extramedullary haematopoiesis of the spleen (National Toxicology Program, 1997).

In a six-month inhalation study, New Zealand White rabbits and Sprague-Dawley rats were exposed by inhalation to 0, 98 or 745 ppm [0, 245 or 1860 mg/m^3] nitromethane for 7 h per day on five days per week for six months. Decreased body weight gain in rats was seen after eight weeks of exposure to 745 ppm. The most notable response in rabbits was an effect on the thyroid: increased thyroid weight and decreased serum thyroxine levels. There were no exposure-related gross or microscopic lesions in either rats or rabbits exposed to 98 or 745 ppm (Lewis *et al.*, 1979).

Male and female Long-Evans (BLU:(LE)BR) rats were exposed by inhalation to 0, 100 or 200 ppm [0, 250 or 500 mg/m^3] nitromethane for 7 h per day on five days per week for two years. Serum chemistry and haematology measurements were not found to be significantly different in nitromethane-exposed rats compared with rats exposed to room air. Body weights of exposed female rats were slightly lower than those of control rats. Tissues weights, however, were unaffected by chronic exposure to nitromethane. Non-neoplastic lesions were not related to nitromethane exposure but in most cases were similar to those found in populations of ageing laboratory rats (Griffin *et al.*, 1996).

In a two-year inhalation study, male and female Fischer 344/N rats and B6C3F$_1$ mice (six weeks of age) were exposed to 0, 94, 188 or 375 ppm [0, 235, 470 or 938 mg/m^3] and 0, 188, 375 or 750 ppm [0, 470, 938 or 1875 mg/m^3] nitromethane, respectively, for 6 h per day on five days per week for 103 weeks. Non-neoplastic lesions that developed with increased incidence included nasal lesions with degeneration and metaplasia of the olfactory epithelium and degeneration of the respiratory epithelium in male and female mice (National Toxicology Program, 1997).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

(*a*) *Developmental toxicity studies*

No data were available to the Working Group.

(*b*) *Reproductive toxicity studies*

In a 13-week inhalation study of nitromethane in male and female Fischer 344/N rats and B6C3F$_1$ mice exposed to 375, 750 or 1500 ppm [938, 1875 or 3750 mg/m^3] for 6 h per day on five days per week, a dose-related decrease in sperm motility was observed. The decrease was significant at doses of 750 and 1500 ppm in rats and at all dose levels in mice. In the 1500-ppm group, body weight as well as weight of cauda, epididymis and testis were decreased in rats. In female mice, estrous cycle length was dose-relatedly increased at all dose levels (National Toxicology Program, 1997).

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 3 for references)

Nitromethane has given consistently negative results in bacterial mutagenicity assays. It also gave negative results in in-vitro mammalian tests for sister chromatid exchanges and chromosomal aberrations. It was not mutagenic in *Drosophila*. It did not induce micronuclei *in vitro* in Syrian hamster embryo cells or *in vivo* in mice. However, nitromethane did show a positive response at high concentration in a cell transformation assay in Syrian hamster embryo cells.

4.5 Mechanistic considerations

The results of short-term tests on nitromethane do not indicate that the compound has genotoxic activity.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Nitromethane is a volatile liquid that is added in small amounts to many halogenated solvents and aerosol propellants as a stabilizer. It is also used as a polar solvent for certain polymers and resins, in specialized fuels and in explosives. Exposures may occur from the use of solvents, propellants and fuels containing nitromethane.

5.2 Human carcinogenicity data

No data were available to the Working Group.

Table 3. Genetic and related effects of nitromethane

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Salmonella typhimurium TA100, TA98, reverse mutation	–	NT	610 µg/plate	Chiu *et al.* (1978)
Salmonella typhimurium TA100, TA1535, TA1537, TA1538, TA98, reverse mutation	–	–	3600 µg/plate	Gocke *et al.* (1981)
Salmonella typhimurium TA100, TA1535, TA98, reverse mutation	–	–	20 000 or 50 000 µg/plate	Löfroth *et al.* (1986)
Salmonella typhimurium TA100, TA1535, TA1537, TA98, reverse mutation	–	–	10 000 µg/plate	Mortelmans *et al.* (1986)
Salmonella typhimurium TA100, TA98, TA102, reverse mutation	–	NT	12 200 µg/plate	Dayal *et al.* (1989)
Salmonella typhimurium TA100, TA98, reverse mutation	NT	–	6100 µg/plate	Dellarco & Prival (1989)
Drosophila melanogaster, sex-linked recessive lethal mutations, Basc test	–		7625 in feed	Gocke *et al.* (1981)
Sister chromatid exchange, Chinese hamster ovary cells *in vitro*	–	–	4965	National Toxicology Program (1997)
Micronucleus test, Syrian hamster embryo cells *in vitro*	–		5000	Gibson *et al.* (1997)
Chromosomal aberrations, Chinese hamster ovary cells *in vitro*	–	–	4980	National Toxicology Program (1997)
Cell transformation, Syrian hamster embryo cells *in vitro*	+		4000	Kerckaert *et al.* (1996)
Micronucleus formation, male and female NMRI mouse bone marrow *in vivo*	–		1830 ip × 2	Gocke *et al.* (1981)
Micronucleus formation, male and female B6C3F_1 mouse peripheral blood erythrocytes *in vivo*	–		1500 ppm by inh × 13 w	National Toxicology Program (1997)

[a] +, positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; inh, inhalation; w, week

5.3 Animal carcinogenicity data

Nitromethane was tested for carcinogenicity by inhalation in one experiment in mice and in two experiments in rats. In mice, it increased the incidence of Harderian gland and lung tumours in males and females as well as of hepatocellular adenomas in females. In one experiment in rats, nitromethane increased the incidence of benign and malignant mammary gland tumours in females, but produced no increase in the incidence of tumours in a second study in a different strain of rat.

5.4 Other relevant data

Nitromethane produces histidinaemia in rats by decreasing hepatic histidase activity, leading to increased tissue levels of histidine.

Neurological effects were observed in nitromethane-exposed rats.

Nitromethane caused mild degeneration of the olfactory epithelium of exposed rats and mice and microcytic anaemia with minimal to mild hyperplasia of the bone marrow in rats.

No data on reproductive or developmental effects in humans were available.

In rats and mice, dose-related decreases in sperm motility were found after inhalation of nitromethane. In females, estrous cycle length was increased in mice but not in similarly exposed rats.

Nitromethane gave negative results in all short-term tests for genetic effects, with the exception of a cell transformation assay in which it was positive at high concentration.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of nitromethane were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of nitromethane.

Overall evaluation

Nitromethane is *possibly carcinogenic to humans (Group 2B).*

6. References

American Conference of Governmental Industrial Hygienists (1999) *TLVs and other Occupational Exposure Values—1999 CD-ROM*, Cincinnati, OH, ACGIH®

Angus Chemical Co. (1998) *Technical Data Sheet: Nitromethane (NM™)*, Buffalo Grove, IL

Archer, W.L. (1996) *Industrial Solvents Handbook*, Chap. 17: Nitroparaffins, NY, Marcel Dekker, pp. 267–282

Budavari, S., ed. (1998) *The Merck Index*, 12th Ed., Version 12:2 [CD-ROM], Whitehouse Station, NJ, Merck & Co.

Chiu, C.W., Lee, L.H., Wang, C.Y. & Bryan, G.T. (1978) Mutagenicity of some commercially available nitro compounds for *Salmonella typhimurium*. *Mutat. Res*., **58**, 11–22

Chemical Information Services, Inc. (1999) *Directory of World Chemical Producers*, Version 99.1.0 [CD-ROM], Dallas, TX

Dahl, A.R. & Hadley, W.M. (1983) Formaldehyde production promoted by rat nasal cytochrome P-450-dependent monooxygenases with nasal decongestants, essences, solvents, air pollutants, nicotine, and cocaine as substrates. *Toxicol. appl. Pharmacol.*, **67**, 200–205

Dayal, R., Gescher, A., Harpur, E.S., Pratt, I. & Chipman, J.K. (1989) Comparison of the hepatoxicity in mice and the mutagenicity of three nitroalkanes. *Fundam. appl. Toxicol*., **13**, 341–348

De Leacy, E.A., Brown, N.N. & Clague, A.E. (1989) Nitromethane interferes in assay of creatinine by the Jaffé reaction. *Clin. Chem*., **35**, 1772–1774

Dellarco, V.L. & Prival, M.J. (1989) Mutagenicity of nitro compounds in *Salmonella typhimurium* in the presence of flavin mononucleotide in a preincubation assay. *Environ. mol. Mutag*., **13**, 116–127

Dequidt, J., Vasseur, P. & Potencier, J. (1973) [Experimental toxicological study of some nitroparaffins. 4. Nitromethane.] *Bull. Soc. Pharm. Lille*, **1**, 29–35 (in French)

Deutsche Forschungsgemeinschaft (1999) *List of MAK and BAT Values 1999* (Report No. 35), Weinheim, Wiley-VCH, pp. 81, XII

Douay, O. & Kamoun, P.P. (1980) Serotonin in experimental histidinemia. *Neurochem. Res*., **5**, 897–903

Dutra-Filho, C.S., Wannmacher, C.M.D., Pires, R.F., Gus, G., Kalil, A.M. & Wajner, M. (1989) Reduced locomotor activity of rats made histidinemic by injection of histidine. *J. Nutr*., **119**, 1223–1227

Eller, P.M., ed. (1994) *NIOSH Manual of Analytical Methods (DHHS (NIOSH) Publ. No. 94-113)*, 4th ed., Cincinnati, OH, National Institute for Occupational Safety and Health [Method 2527]

Gibson, D.P., Brauninger, R., Shaffi, H.S., Kerckaert, G.A., LeBoeuf, R.A., Isfort, R.J. & Aardema, M.J. (1997) Induction of micronuclei in Syrian hamster embryo cells: comparison to results in the SHE cell transformation assay for National Toxicology Program test chemicals. *Mutat. Res*., **392**, 61–70

Gocke, E., King, M.-T., Eckhardt, K. & Wild, D. (1981) Mutagenicity of cosmetics ingredients licensed by the European Communities. *Mutat. Res*., **90**, 91–109

Griffin, T.B., Coulston, F. & Stein, A.A. (1996) Chronic inhalation exposure of rats to nitromethane. *Ecotoxicol. environ. Saf*., **34**, 109–117

Hansch, C., Leo, A. & Hoekman, D. (1995) *Exploring QSAR: Hydrophobic, Electronic, and Steric Constants*, Washington DC, American Chemical Society, p. 3

Kaiffer, M., Helmer, J., Jacob, F., Geneftet, B. & Larcan, A. (1972) [Acute toxic methaemoglobinaemia with anuria after use of nitrocellulose and nitromethane.] *Nouv. Presse méd*., **1**, 55–57 (in French)

Kerckaert, G.A., Brauninger, R., LeBoeuf, R.A. & Isfort, R.J. (1996) Use of the Syrian hamster embryo cell transformation for carcinogenicity prediction of chemicals currently being tested by the National Toxicology Program in rodent bioassays. *Environ. Health Perspect.*, **104** (Suppl. 5), 1075–1084

Lee, S.-C. & Wang, M-L. (1975) Histidinemia produced in the rat by treatment with nitromethane. *Nutr. Metab*., **18**, 79–88

Lewis, T.R., Ulrich, C.E. & Busey, W.M. (1979) Subchronic inhalation toxicity of nitromethane and 2-nitropropane. *J. environ. Pathol. Toxicol*., **2**, 233–249

Lide, D.R. & Milne, G.W.A. (1996) *Properties of Organic Compounds*, Version 5.0 [CD-ROM], Boca Raton, FL, CRC Press

Löfroth, G., Nilsson, L. & Andersen, J.R. (1986) Structure–activity relationship of nitroalkane-induced mutagenicity in the Ames Salmonella assay. Genetic toxicology of environmental chemicals, Part B: Genetic effects and applied mutagenesis. *Prog. clin. biol. Res*., **209B**, 149–155

Lundberg, P. (1989) Consensus report for nitromethane. *Arbete och Halsa*, **32**, 86–91

Markofsky, S. (1991) Nitro compounds, aliphatic. In: Elvers, B., Hawkins, S. & Schulz, G., eds, *Ullmann's Encyclopedia of Chemical Technology*, 5th Rev. Ed., Vol. A17, New York, VCH Publishers, pp. 401–409

Ministry of Social Affairs and Health (1998) *Finnish Occupational Exposure Limits 1998. Concentrations Known to be Harmful*. [http://www.occuphealth.fi]oel_eng.htm

Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B. & Zeiger, E. (1986) *Salmonella* mutagenicity tests: II. Results from the testing of 270 chemicals. *Environ. Mutag*., **8**, 1–119

Mullins, M.E. & Hammett-Stabler, C.A. (1998) Intoxication with nitromethane-containing fuels: don't be 'fueled' by the creatinine. *Clin. Toxicol*., **36**, 315–320

National Library of Medicine (1999) *Hazardous Substances Data Bank*, Bethesda, MD

National Toxicology Program (1997) *Toxicology and Carcinogenicity Studies of Nitromethane (CAS No. 75-52-5) in F344 Rats and B6C3F$_1$ Mice (Inhalation Studies)* (Technical Report Series No. 461; NIH Publication No. 97-3377), Research Triangle Park, NC

NOES (1999) *National Occupational Exposure Survey (1981 to 1983)*. Unpublished data as of July 1999. Cincinnati, OH, Department of Health and Human Services, Public Health Service, National Institute for Occupational Safety and Health

Occupational Safety and Health Administration (1999) Labor. *US Code Fed. Regul*., **Title 29**, Part 1910, Subpart 1910.1000, pp. 7–19

Pellizzari, E.D., Hartwell, T.D., Harris, B.S.H., III, Waddell, R.D., Whitaker, D.A. & Erickson, M.D. (1982) Purgeable organic compounds in mother's milk. *Bull. environ. Contam. Toxicol*., **28**, 322–328

Sadtler Research Laboratories (1980) *Sadtler Standard Spectra*, 1980 Cumulative Index (Molecular Formula Index), Philadelphia, PA, p. 2

Sandyk, R. & Gillman, M.A. (1984) Motor dysfunction following chronic exposure to a fluoroalkane solvent containing nitromethane. *Eur. Neurol*., **23**, 479–481

Seizinger, D.E. & Dimitriades, B. (1972) Oxygenates in exhaust from simple hydrocarbon fuels. *J. Air Poll. Control Assoc.*, **22**, 47–51

Verschueren, K. (1996) *Handbook of Environmental Data on Organic Chemicals*, 3rd Ed., New York, Van Nostrand Reinhold, p. 1393

Wade, A.E., Evans, J.S., Sternson, L.A. & Gammans, R.E. (1977) Interaction of nitromethane with reduced hepatic microsomal cytochrome P 450. *Biochem. Pharmacol.*, **26**, 963–967

Zitting, A., Nickels, J. & Savolainen, H. (1982) Comparison of acute toxic effects of intraperitoneally injected nitromethane and nitroethane in rats. *Toxicol. Lett.*, **13**, 189–194