The MAK Collection for Occupational Health and Safety

1-Nitropropane

MAK Value Documentation, addendum – Translation of the German version from 2017

A. Hartwig[1,*], MAK Commission[2,*]

1 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

2 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

***** *email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

Keywords: 1-nitropropane; MAK value; maximum workplace concentration; peak limitation; skin absorption; irritation; nose; inflammation

Citation Note: Hartwig A, MAK Commission. 1-Nitropropane. MAK Value Documentation, addendum – Translation of the German version from 2017. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2019 Jan;4(1):51-72]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2025. https://doi.org/10.34865/mb10803e6319_w

Republished (online): 08 Aug 2025

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.mb10803e6319

Addendum completed: 24 Feb 2016

Published (online): 30 Jan 2019

The commission established rules and measures to avoid conflicts of interest.

1-Nitropropane[1)]

MAK Value Documentation

A. Hartwig[1,*], MAK Commission[2,*]

DOI: 10.1002/3527600418.mb10803e6319

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the maximum concentration at the workplace (MAK value) for 1-nitropropane, considering all toxicity endpoints. The critical effects of 1-nitropropane [108-03-2] were inflammation and degeneration of the olfactory mucosa and inflammation of the squamous epithelium in rats after 28 or 47 days inhalation. The study yielded a NOAEC of 24 ml/m³ for local effects. Since 2014, the Commission uses an empirical approach to set MAK values for substances with critical effects on the upper respiratory tract or the eyes. According to this approach, the MAK value for 1-nitropropane has been lowered from 25 ml/m³ to a concentration of 2 ml/m³. As local effects are critical, the assignment to Peak Limitation Category I is confirmed. The excursion factor of 8 is set as a human volunteer study revealed irritative effects only at considerably higher concentrations. Because there are no studies of teratogenicity, the substance is classified in Pregnancy Risk Group D. Skin contact is expected to contribute significantly to systemic toxicity and 1-nitropropane is designated with an "H". 1-Nitropropane is not genotoxic and data for carcinogenicity are lacking. Sensitization is not expected from the limited data.

Keywords

1-nitropropane; mechanism of action; toxicokinetics; metabolism; (sub)acute toxicity; (sub) chronic toxicity; irritation; allergenic effects; reproductive toxicity; fertility; developmental toxicity; genotoxicity; carcinogenicity; peak limitation; prenatal toxicity; germ cell mutagenicity; absorption through the skin; sensitization; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

Author Information

[1] Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany

[2] Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

* Email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

1) Technical products measurably contaminated with 2-nitropropane, see 2-Nitropropane.

1-Nitropropane[1)]

[108-03-2]

Supplement 2017

MAK value (2016)	**2 ml/m³ ≙ 7.4 mg/m³**
Peak limitation (2016)	**Category I, excursion factor 8**
Absorption through the skin (2016)	**H**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2016)	**Pregnancy Risk Group D**
Germ cell mutagenicity	**–**
BAT value	**–**
Vapour pressure at 25 °C	13.3 hPa (ECB 2000)
log Kow[2)]	0.79 (ECHA 2015)
Solubility in water	15 g/l (ECHA 2015)
1 ml/m³ (ppm) ≙ 3.697 mg/m³	**1 mg/m³ ≙ 0.271 ml/m³ (ppm)**

In 1997 the MAK value from 1963 was confirmed for 1-nitropropane on the basis of new data (documentation "1-Nitropropane" 1999) and an excursion factor was set in 2000 (supplement "1-Nitropropan" 2000, available in German only). This supplement was drawn up because a new inhalation study is now available.

1 Toxic Effects and Mode of Action

1-Nitropropane is slightly irritating to the eyes of humans and rabbits. It is not irritating to the skin of rabbits.

1) Technical products measurably contaminated with 2-nitropropane, see 2-Nitropropane.

2) octanol/water partition coefficient.

In a screening study with inhalation exposure of rats, the main effects were degeneration and inflammation of the olfactory epithelium and of the squamous epithelium in the nose at concentrations of 48 ml/m^3 and above. In this study, reductions in food consumption and body weights were first observed at a concentration of 96 ml/m^3.

The reduced body weight gains and food consumption found in rats after oral 1-nitropropane doses of 30 mg/kg body weight and above are attributed to irritation caused by gavage administration.

Reduced litter sizes were found in a screening study with rats at the highest concentration tested of 96 ml/m^3 after exposure for 47 days.

1-Nitropropane is not sensitizing to the skin and does not have genotoxic or carcinogenic potential.

2 Mechanism of Action

The relatively low liver toxicity of 1-nitropropane compared with that of 2-nitropropane and the absence of carcinogenicity could be explained by the rapid absorption, metabolism and elimination of the substance (Haas-Jobelius et al. 1989).

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

1-Nitropropane can be absorbed via the gastrointestinal tract and via the lungs. Some of it is eliminated with the urine in unchanged form. Nitrite, a metabolite of nitropropane, is eliminated with the urine in the form of nitrate (NLM 2006).

After 5 male rats were given single intraperitoneal doses of 1-[1-^{14}C]nitropropane of 40 mg/kg body weight, 16.5% of the radioactivity was eliminated with the urine and 1.7% with the faeces after 48 hours. The major route of elimination was via the lungs; 72.6% of the radioactivity was exhaled (of which 10.3% was in unchanged form), with a maximum amount after 12 to 16 minutes and an elimination half-life of 55.4 ± 9.3 minutes. A further 6% to 7% of the radioactivity was recovered in the organs and the bones. The highest levels of radioactivity were found in the liver, stomach, kidneys and bone marrow. Many other organs were found to have radioactivity levels similar to those of the plasma (Haas-Jobelius et al. 1989).

In chimpanzees given a single intravenous injection of 1-[1-^{14}C]nitropropane of 5 mg/kg body weight, 14.8% of the radioactivity was eliminated with the urine and 1.2% with the faeces. The authors did not provide any data for exhalation via the lungs (see Section 3.2; Haas-Jobelius et al. 1989).

Extracted human skin was heat-treated and the epidermis tested in a static diffusion cell. The receptor fluid consisted of saline with 6% polyethylene glycol 20-oleyl ether. To determine the penetration rate at steady state, a non-exhaustible dose of undiluted 1-nitropropane of 1200 µl/cm^2 was used. To determine the short-term fluxes after 10 and 60 minutes, 20 µl/cm^2 was used. The penetration rate at steady state was 180 µg/cm^2 and hour. The penetration rate was 1218.5 µg/cm^2 and hour

after 10 minutes, and 178.9 µg/cm² and hour after 60 minutes (Dow Chemical Company 1989; Fasano and McDougal 2008). From the latter value, an absorbed amount of 358 mg is calculated for an exposed skin surface of 2000 cm² and exposure for one hour. The value is probably an overestimation, as the electrical resistance of the skin after application was only half as high as it was prior to the application, which indicates a certain amount of damage to the skin. Furthermore, the authors assume that the polyethylene glycol ether in the receptor phase acted as a penetration accelerator.

For a saturated aqueous solution, fluxes of 236, 28 or 44 µg/cm² and hour are obtained using the models of Fiserova-Bergerova et al. (1990), Guy and Potts (1993) and Wilschut et al. (1995). Assuming the exposure of 2000 cm² of skin for one hour, this would correspond to absorbed amounts of 472, 56 and 88 mg, respectively.

Therefore, the 358 mg obtained in the in vitro study do not contradict the absorbed amounts calculated according to these models.

3.2 Metabolism

Primary aliphatic nitro compounds can be hydroxylated, whereby the corresponding aldehyde is formed from the hypothetically produced geminal hydroxy-nitro intermediate resulting in the release of nitrite (Ullrich et al. 1978). Nitroalkanes oxidize only slowly. The following pathway is proposed for the oxidative metabolic degradation of 1-nitropropane (Figure 1; Lai et al. 1982):

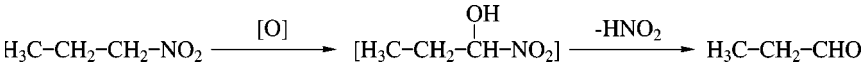

Figure 1 Oxidative metabolic degradation of 1-nitropropane

In vitro studies with liver microsomes of rats showed that nitroalkanes can be denitrified by means of a microsomal cytochrome P450 monooxygenase system and different flavoenzyme oxidases (Davis 1993; Stokinger 1982).

The inhalation exposure of rats to 1-nitropropane led to the slight induction of cytochrome P450 enzymes (22%–28%), whereas exposure to 2-nitropropane caused a decrease in cytochrome P450 enzymes. An intermediate responsible for the inhibition of the cytochrome P450 system by 2-nitropropane is possibly not formed here (see Section 5.2.1; Haas-Jobelius et al. 1992).

The oxidative denitrification of 1-nitropropane by phenobarbital-induced rat liver microsomes took place at a rate of 0.6 nmol/minute and mg protein. Therefore, the reaction was slower than the denitrification of the homologous secondary nitroalkane 2-nitropropane, which was metabolized at a rate of 2.4 nmol/minute and mg protein. The rate was determined via nitrite formation (Ullrich et al. 1978).

Nitro compounds can be reduced to hydroxylamine or amine by nitroreductases. The presence of nitroreductases has been demonstrated in bacteria and in the liver of mammals (Williams et al. 1989). The reductive metabolism can lead to metHb formation which, to a small extent, was found in rats after 1-nitropropane administration (Dow Chemical Company 1996).

In 5 male rats given a single intraperitoneal dose of 1-[1-^{14}C]nitropropane of 40 mg/kg body weight, 72.6% of the absorbed amount was exhaled, 10.3% of which as the unchanged substance. The main product of exhalation was $^{14}CO_2$, whereas propionaldehyde, like the main metabolite acetone of 2-nitropropane, could not be detected. The main metabolites in the urine were 3-hydroxypropionic acid (12% of the total amount eliminated with the urine) and *N*-methyl-*N*-2-(methylsulfinyl)ethylpropionic acid (6% of the total amount eliminated with the urine). The other five metabolites could not be identified (Haas-Jobelius et al. 1989).

After intravenous injection of a single 1-[1-^{14}C]nitropropane dose of 5 mg/kg body weight, five metabolites were identified in the urine of chimpanzees. The main metabolites were 3-hydroxypropionic acid (25% of the total amount eliminated with the urine) and *N*-methyl-*N*-2-(methylsulfinyl)ethylpropionic acid (30% of the total amount eliminated with the urine). The detection of these two metabolites indicates that, in the first step, 1-nitropropane is degraded to form propionic acid and the propionic acid is then modified to 3-hydroxypropionic acid or *N*-methyl-*N*-2-(methylsulfinyl)ethylpropionic acid amide. The other metabolites could not be characterized. The authors did not provide any data for exhaled air (see Section 3.1; Haas-Jobelius et al. 1989).

After intraperitoneal injection in rats and intravenous injection in chimpanzees, the biotransformation of 1-nitropropane may lead to the accumulation of unusually high levels of propionic acid or propionyl-CoA. In turn, as a result of a propionate overload and the saturation of metabolic pathways, reactions could take place resulting in the presence of the demonstrated metabolites. The β-oxidation or ω-oxidation of propionyl-CoA with subsequent hydrolysis may lead to the formation of the 3-hydroxypropionic acid found in the urine. The pathway by which the main urinary metabolite *N*-methyl-*N*-2-(methylsulfinyl)ethylpropionic acid amide is formed is not known (see Section 3.1; Haas-Jobelius et al. 1989).

At a pH of 7.4, the equilibrium between propane-1-nitronate and 1-nitropropane is shifted in favour of 1-nitropropane, which then makes up 95% of the amount (Linhart et al. 1991).

4 Effects in Humans

There are no data available for the end points allergenic effects, reproductive toxicity and genotoxicity.

4.1 Single exposures

In a study from 1946, irritation of the eyes but not of the nose or throat occurred in 12 female and 12 male volunteers after a 15-minute exposure to 1-nitropropane concentrations of 150 ml/m^3 and above. The volunteers considered a concentration of 100 ml/m^3 to be tolerable (documentation "1-Nitropropane" 1999; supplement "1-Nitropropan" 2000, available in German only; Silverman et al. 1946).

The odour threshold of 1-nitropropane is 11 ± 4.2 ml/m^3 (Bingham et al. 2001).

4.2 Repeated exposure

In a study with 1481 workers from a factory producing nitromethane, nitroethane, 1-nitropropane and 2-nitropropane, which covered the period between 01/01/1946 and 31/12/1981, there was no evidence of an increase in diseases (no other details; ECB 2000).

4.3 Local effects on skin and mucous membranes

In volunteers, irritation of the eyes occurred after a 15-minute exposure to 1-nitropropane concentrations of 150 ml/m³ and above (Silverman et al. 1946).

4.4 Carcinogenicity

A mortality study with 1481 workers from a factory producing nitromethane, nitroethane, 1-nitropropane and 2-nitropropane, which covered the period between 01/01/1946 and 31/12/1981, provided no evidence of an increased number of tumours or cases of rare tumours leading to mortality (no other details; ECB 2000).

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

The LC_{50} for the rat after inhalation exposure for one hour was found to be 3024 ml 1-nitropropane/m³. The purity of the substance was 96.12% with 2.44% 2-nitropropane (Dow Chemical Company 1981). The LC_{50} after one-hour inhalation exposure of female Wistar rats was 5500 mg 1-nitropropane/m³ (about 1500 ml/m³, purity 96%) (ECHA 2015).

After exposure to 1-nitropropane concentrations of 13 000 ml/m³ (48 000 mg/m³) for 5 hours and 2500 ml/m³ (9200 mg/m³) for 8 hours, 8.5% and 4.1% methaemoglobin was found in the blood of Wistar rats, respectively. Exposure to a 1-nitropropane concentration of 1100 ml/m³ (4000 mg/m³) for 11 hours did not increase the methaemoglobin level (Dequidt et al. 1972).

Groups of 2 rabbits and 2 guinea pigs were exposed to 1-nitropropane concentrations of 5000 or 9800 ml/m³ for 3 hours. All animals died. At the high concentration, exposure for one hour already resulted in the death of one guinea pig. Visceral and cerebral congestion and pulmonary congestion with oedema were diagnosed in these animals. Clear signs of irritation were observed in the upper respiratory tract. In addition, liver damage was found in all of the animals. In these studies, the toxicity of 1-nitropropane was found to be greater than that of nitroethane and nitromethane (Machle et al. 1940).

5.1.2 Oral administration

In groups of 10 female or 10 male Sprague Dawley rats given gavage doses of 0, 290, 360, 450 or 570 mg/kg body weight, LD_{50} values of 528 mg/kg body weight were obtained in the males and 484 mg/kg body weight in the females. Convulsions and ataxia occurred, and distended and haemorrhagic intestines were found. At doses of 290 mg/kg body weight and above, lung infections were observed (Dow Chemical Company 1981; ECHA 2015).

The oral LD_{50} for rats was between 280 and 530 mg 1-nitropropane/kg body weight (ECHA 2015; Zitting 1988).

The oral LD_{50} was between 250 and 500 mg/kg body weight for rabbits (Machle et al. 1940; NTP 2014).

5.1.3 Dermal application

Even after 5 days, 4-hour open application of 1-nitropropane to the shaved skin did not produce effects (no other details; Machle et al. 1940).

The dermal LD_{50} was greater than 2000 mg/kg body weight in rabbits (Dow Chemical Company 1981).

5.1.4 Intraperitoneal injection

After intraperitoneal injection, the LD_{50} was 250 mg/kg body weight in mice. The lethal dose was 505 mg/kg body weight. Increased levels of methaemoglobin and carboxyhaemoglobin were found in the blood (no other details; NIOSH 2003).

In another study, the lethal dose in rats was 550 mg/kg body weight. A level of 4% methaemoglobin was determined in the blood (Dequidt et al. 1972).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

Male Sprague Dawley rats were exposed whole-body to 1-nitropropane concentrations of 0 or 100 ml/m^3 for 7 hours on 4 consecutive days. There were 9 animals in each group, 3 of which per group were examined after 1, 2 and 4 days. The glutathione (GSH) level was not increased. The determination of the liver enzymes revealed significantly increased levels of activity for cytochrome P450 (by 22%–28%), cytochrome b_5 and GSH peroxidase on days 1 and 2, and an increase in GSH S-transferase activity at all three examinations that was not significant. The GSSG reductase activity was slightly decreased. The level of malondialdehyde, a product of lipid peroxidation, did not increase compared with that in controls. The activity of UDP glucuronosyl transferase in the liver and of aspartate aminotransferase and alanine aminotransferase in the serum was unchanged. No further parameters were examined (Haas-Jobelius et al. 1992).

In a range-finding study for the screening study according to OECD Test Guideline 422, groups of 5 female and 5 male Sprague Dawley rats were exposed whole-body to 1-nitropropane concentrations of 0, 100, 250 or 500 ml/m^3 for 6 hours per

day, on 7 days per week. The 1-nitropropane concentrations determined in the exposure chamber were 0, 84.9 ± 2.4, 225.4 ± 8.4 or 356.0 ± 9.3 ml/m³. The effects are described in Table 1. At concentrations of 225.4 ml/m³ and above, the animals were moribund. Delayed body weight gains and reduced food consumption were observed. The decrease in relative weights of the liver and kidneys correlated with the reduced body weights (Dow Chemical Company 2004). In this range-finding study there were no histopathological examinations of the organs, or of the target organ, the nose.

In a screening study carried out according to OECD Test Guideline 422, groups of 12 female and 12 male Sprague Dawley rats were exposed whole-body to 1-nitropropane concentrations of 0, 25, 50 or 100 ml/m³ for 6 hours per day, on 7 days per week. The animals were mated after 14 days and the females exposed up to gestation day 19 (day 47). The exposure period was 28 days for the male rats. The exposure atmosphere consisted of vapour. The purity of the 1-nitropropane was 99.69%. The mean concentrations in the chamber were 0, 24.4 ± 1.8, 48.4 ± 1.8 or 96.3 ± 2.6 ml/m³. The effects found are listed in Table 1. The findings for haematological and clinico-chemical parameters were normal. Functional tests revealed no differences between the exposed animals and the controls. The decrease in the absolute and relative thymus weights in the male rats was not concentration-dependent at the concentration of 24 ml/m³. Methaemoglobin levels were not affected. Minimal concentration-dependent increases in heart weights were interpreted by the authors as not relevant, as they were not statistically significant and no histopathological changes were found in the heart. Degeneration of the olfactory epithelium and inflammatory processes in the squamous epithelium of the nasal cavity were seen in the female animals at 48.4 ml/m³ and above. The NOAEC (no observed adverse effect concentration) was 24.4 ml 1-nitropropane/m³ for female rats and 48.4 ml/m³ for the males. The individual data for the effects in the nasal tissue are given in Table 2. The results of the investigation of reproductive toxicity in the study are described in Section 5.5 (Dow Chemical Company 2004). With a respiratory volume of 0.8 l/min/kg body weight and 100% absorption, a dose of 100 mg/kg body weight and day is obtained for exposure to 96.3 ml/m³ for 6 hours.

In the evaluation it must be taken into account that in rats 15% and in humans 7% of the inhaled air reaches the olfactory epithelium (Frederick et al. 1998).

Groups of 125 male and 125 female Long Evans rats were exposed to 1-nitropropane concentrations of 0 or 101 ml/m³ for up to 21.5 months. Gross-pathological and histopathological examinations of the liver did not yield any abnormal findings. The kidney and brain weights were unchanged. In the serum, no effects were found after clinico-chemical analysis. Haematological examination did not reveal any increase in methaemoglobin, haemoglobin and haematocrit values, or unusual changes in erythrocyte and leukocyte counts and prothrombin time. This study is available as a publication but there are no further data for 25 microscopically examined organs. Furthermore, there are no data as to whether the upper respiratory tract, in particular the nose as target organ, was also examined (documentation "1-Nitropropane" 1999; Griffin et al. 1982).

Table 1 Effects of 1-nitropropane repeated after inhalation

Species, strain, number per group	Exposure	Findings	References
rat, Sprague Dawley, 9 ♂	**4 days**, 0, 100 ml/m^3 7 hours/day	**100 ml/m^3**: liver enzyme activity ↑ examination limited to liver enzyme activity	Haas-Jobelius et al. 1992
rat, Sprague Dawley, 5 ♀, 5 ♂	**14 days**, 0, 85, 225, 356 ml/m^3 6 hours/day, 7 days/week (range-finding study)	**85 ml/m^3**: **NOAEC** body weight gains ↓ (by 4%); **225 ml/m^3 and above**: body weight gains ↓ (by 15%), terminal body weights compared with those of the controls and food consumption ↓, absolute and relative liver weights ↓, absolute and relative kidney weights ↓ ♀: unsteady gait (3/5), faeces volume ↓ (4/5), perioral and periocular contamination (2/5), 2 animals killed (day 10); **356 ml/m^3**: ♂: 3 animals died (days 3–4), 2 animals moribund, ♀: all animals moribund (day 5)	Dow Chemical Company 2004

Table 1 (continued)

Species, strain, number per group	Exposure	Findings	References
rat, Sprague Dawley, 12 ♀, 12 ♂	♂**: 28 days**, ♀**: 47 days**, up to gestation day 19 0, 24, 48, 96 ml/m³ 6 hours/day, 7 days/week	**24 ml/m³**: ♀**: NOAEC** ♂: absolute and relative thymus weights ↓* (not concentration-dependent); **48 ml/m³ and above**: ♂: **NOAEC** ♀: nasal cavity: degeneration of the olfactory epithelium (2/12 minimal), chronic inflammation of squamous epithelium (3/12), AP ↑; **96 ml/m³**: food consumption ↓*, relative heart weights ↑, AST ↓, nasal cavity: degeneration of olfactory epithelium (♂: 1/12, ♀: 9/12), chronic inflammation of squamous epithelium (♂: 1/12, ♀: 4/12), ♂: body weights ↓* (from day 7), relative brain weights ↑*, relative testis weights ↑*, albumin ↑, ♀: K^+ ↓ (urine)	Dow Chemical Company 2004
rat, Long Evans, 125 ♀, 125 ♂	**1, 3, 12, 18, 21.5 months**, 0, 101 ml/m³ 7 hours/day, 5 days/week	**101 ml/m³**: **NOAEC** nasal cavity not examined	Griffin et al. 1982

*$p < 0.05$; AP: alkaline phosphatase
AST: aspartate aminotransferase; K^+: potassium ions

Table 2 Treatment-related effects of 1-nitropropane in the nasal tissue (Dow Chemical Company 2004)

	male				female			
Concentration (ml/m³)	0	24	48	96	0	24	48	96
number of animals	12	12	12	12	12	12	12	12
degeneration, olfactory epithelium, multifocal								
minimal				**1**				**5**
slight				**1**				**2**
degeneration, with inflammation, olfactory epithelium, focal								
minimal							**2**	
degeneration, with inflammation, olfactory epithelium, multifocal								
slight								**2**
inflammation, chronically active, squamous epithelium, focal								
minimal					2	1		
slight								**1**
inflammation, chronically active, squamous epithelium, multifocal								
minimal					1	1	1	2
slight				**1**			**2**	**1**

Values in bold print are considered as treatment-related and adverse.

Summary

In rats, in a screening study according to OECD Test Guideline 422, irritation of the olfactory and squamous epithelium was found to be the most sensitive end point, which increased in a concentration-dependent manner with increasing exposure duration. The NOAEC was 24 ml 1-nitropropane/m³ for female rats and 48 ml/m³ for the males. The NOAEC for systemic effects (delayed body weight gains, reduced food consumption) was 48 ml/m³.

5.2.2 Oral administration

In a study carried out according to OECD Test Guideline 422, which was discontinued after 8 days due to severe toxicity, groups of 12 female and 12 male Sprague Dawley rats were given daily 1-nitropropane doses of 0, 10, 50 or 90 mg/kg body weight by gavage. Marked effects were seen in the males even at 50 mg/kg body weight, whereas decreased body weights and reduced food consumption were not observed in the females until 90 mg/kg body weight. The results are shown in Table 3 (no other details; Dow Chemical Company 2004).

Table 3 Effects of 1-nitropropane after repeated oral administration

Species, strain, number per group	Exposure	Findings	References
rat, Sprague Dawley, 12 ♂, 12 ♀	**8 days**, 0, 10, 50, 90 mg/kg body weight and day, gavage, discontinued after 8 days	**50 mg/kg body weight and above**: ♂: body weights ↓*, food consumption ↓*, perioral contamination due to excessive salivation (4/12), reactivity ↓ (2/12, no other details); **90 mg/kg body weight**: body weights ↓**, food consumption ↓**, ♂: activity ↓, enlarged and protruding eyes, uncoordinated gait, dragging of hindquarters, front limbs bent, perioral and periocular contamination, 2 animals moribund	Dow Chemical Company 2004
rat, Fischer 344, 10 ♂	**14 days**, 0, 20, 40, 80 mg/kg body weight and day, gavage, 10×/day, 5 days/week dissolved in 10% Emulphor EL-620	**20 mg/kg body weight and above**: albumin ↑*; **40 mg/kg body weight and above**: triglycerides ↓; **80 mg/kg body weight**: body weights ↓*, food consumption ↓*, AP ↓, alanine transaminase ↑*, triglycerides ↓*	Cunningham and Matthews 1991
rat, Sprague Dawley, 3 ♂, 3 ♀	**14 days**, 0, 10, 50, 100, 150, 250 mg/kg body weight and day, gavage, 7 days/week, substance dissolved in arachis oil, range-finding study, discontinued after 8 days	**50 mg/kg body weight**: unkempt coat (1/6), pale kidneys (4/6); **150 mg/kg body weight**: day 7: 1 ♂ moribund, piloerection, paleness of extremities, ataxia, body tremor, absent reflex (1 animal), perioral contamination due to increased salivation (2 animals), necropsy: pale kidneys, pink-coloured testicular fat, thickening of the non-glandular region of the stomach; **250 mg/kg body weight**: day 4: 2 animals moribund, day 9: all animals moribund, body weights ↓, hunched posture, decreased respiration, ptosis, paleness of extremities, ataxia, dehydration, emaciation, reflex loss, necropsy: pale liver, pale kidneys and adrenal glands, epithelial sloughing in the glandular region of the stomach	Dow Chemical Company 1996

Table 3 (continued)

Species, strain, number per group	Exposure	Findings	References
rat, Sprague Dawley, 5 ♂, 5 ♀	**28 days**, 0, 10, 30, 100 mg/kg body weight and day, gavage, 7 days/week, substance dissolved in arachis oil	**controls**: metHb ♂: 0.87%, ♀: 0.47%; **10 mg/kg body weight**: blood: metHb ↑ (♂: 2.67%*, ♀: 0.54%), ♂: urine: Hb (1/5; 5–10 × 10^6 WBC/l, no other details), AP ↓, ♀: absolute weights of adrenal glands ↑**, relative weights of adrenal glands ↑*, absolute heart weights ↑*, AP ↓*; **30 mg/kg body weight**: blood: metHb (♂: 0.94%, ♀: 0.93%), relative heart weights ↑, ♂: body weights ↑*, absolute liver weights ↑*, urine: Hb (1/5; 5–10 × 10^6 WBC/l, no other details), AP ↓, ♀: absolute brain weights ↑*; relative brain weights ↑; AP ↓; **100 mg/kg body weight**: body weight gains ↓*, food consumption ↓, salivation ↑, hunched posture (3/10), blood: metHb ↑ (♂: 1.19%, ♀: 1.28%); AP ↓, ♂: 1 animal died on day 27 (kidneys: dark discoloration, stomach: extremely thickened non-glandular region, epithelial sloughing of the glandular region), urine (1/5; 50 × 10^6 WBC/l, no other details) absolute pituitary weights ↓*, absolute brain weights ↑*, relative brain weights ↑**, relative heart weights ↑**, relative kidney weights ↑, ♀: absolute brain weights ↑***, relative brain weights ↑, absolute kidney weights ↑*, absolute ovary weights ↓, relative ovary weights ↓*, relative kidney weights ↑**, relative liver weights ↑, relative heart weights ↑	Dow Chemical Company 1996

Table 3 (continued)

Species, strain, number per group	Exposure	Findings	References
rat, Sprague Dawley, 5 ♂, 5 ♀	**28 days and 14 days recovery period**, satellite group, 0, 100 mg/kg body weight and day, 7 days/week, gavage, substance dissolved in arachis oil	**100 mg/kg body weight**: ♀: relative heart weights ↑ (by 11%), relative liver weights ↓ (by 6%)	Dow Chemical Company 1996
rat, Sprague Dawley, ♂, number of animals not specified (> 26)	**26 weeks**, **77 weeks recovery period**, 0, 89 mg/kg body weight, 3 days/week (16 weeks), 1 day/week (10 weeks), = about 40 mg/kg body weight and day on average, gavage, substance dissolved in 10% Emulphor EL-620	**40 mg/kg body weight**: body weight gains ↓, (control values regained during recovery period), liver weights ↑, liver spotted and reticular, no other details	Fiala et al. 1987

*p < 0.05; **p < 0.01; ***p < 0.001
AP: alkaline phosphatase; Hb: haemoglobin; WBC: white blood cells

In a study comparing 1-nitropropane and 2-nitropropane, 1-nitropropane doses of 0, 20, 40 or 80 mg/kg body weight and day were administered by gavage in 10 portions/day to groups of 10 male F344 rats for 14 days. The purity of the substance was > 98% and it was dissolved in 10% Emulphor EL-620. The effects are given in Table 3. No other organs were examined (Cunningham and Matthews 1991).

In a range-finding study for the 28-day gavage study in which groups of 3 female and 3 male Sprague Dawley rats were given 1-nitropropane doses of 0, 10, 50, 150 or 250 mg/kg body weight and day in arachis oil, all high-dose animals were moribund after 9 days as was one animal in the 150 mg/kg group after 7 days. The other observations are given in Table 3 (Dow Chemical Company 1996).

In groups of 5 female and 5 male Sprague Dawley rats, daily gavage administration over a period of 28 days of 1-nitropropane doses of 0, 10, 30 or 100 mg/kg body weight and day in arachis oil produced minor effects in the liver, kidneys, heart and the haematopoietic system at the low dose and above. In the high dose group, body weights were decreased and food consumption reduced. The effects are listed in Table 3. As a result of the increase in brain weights in the high dose group, microscopic examination of brain sections was carried out, which, however, did not reveal any treatment-related changes. The authors regarded the effects in the low and middle dose groups as not toxicologically relevant or as not substance-related because of the lack of dose-dependency (Dow Chemical Company 1996).

In a carcinogenicity study, male Sprague Dawley rats were given gavage doses of 1-nitropropane of 0 or 89 mg/kg body weight. The substance was administered on 3 days per week for 16 weeks, and subsequently once a week for 10 weeks, followed by a 77-week recovery period. The exact number of animals is not specified. Twenty-six animals survived. There was no increase in tumor incidence. Body weight gains were only initially reduced. In addition, decreased liver weights were observed, as given in Table 3 (no other details; Fiala et al. 1987).

Summary

In the gavage studies with repeated administration, a significant decrease in body weights and reduced food consumption were found at 80 mg/kg body weight and above. However, these effects were reversible during the recovery period. A clear dose-dependent systemic effect is not evident. The effects found can be attributed to irritation after gavage administration.

After 28-day treatment with 1-nitropropane, increased methaemoglobin levels in the male rats and increased adrenal gland and heart weights in the females were observed at 10 mg/kg body weight and day; these changes were, however, not dose-dependent. In animals given 100 mg/kg body weight and day, the absolute and relative brain weights were increased, though without any histopathological correlate. The sporadic increases in other organ weights also occurring in the higher dose groups were not dose-dependent.

5.2.3 Dermal application

No studies with dermal application of 1-nitropropane are available.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

In undiluted form and under occlusive conditions, 0.5 ml 1-nitropropane (2.44% 2-nitropropane; 0.64% 1-nitro-2-methylpropane; 0.42% 2-nitrobutane; 0.35% 2-nitro-2-methylpropane; 0.013% water, all data in % by weight) was applied to the shaved intact and abraded skin of 6 albino rabbits for 24 hours. No effects were found on either the intact or abraded skin 72 hours after the exposure (irritation index 0) (Dow Chemical Company 1981; ECHA 2015).

The application of 0.5 ml 1-nitropropane (96.12%) to the intact skin of 6 albino rabbits under occlusive conditions for 4 hours did not cause irritation 4, 24 and 48 hours after application (ECHA 2015).

In another study, slight irritation was reported after application of the substance to the intact and abraded skin of rabbits (no other details; ECHA 2015).

5.3.2 Eyes

The instillation of 0.1 ml undiluted 1-nitropropane into the conjunctival sac of the eyes resulted in moderately excessive lacrimation in only one of 6 albino rabbits after 48 and 72 hours. In this study, the eye was held closed for one second after application. No other irritant effects occurred (Dow Chemical Company 1974).

In another study, 0.1 ml 1-nitropropane was instilled into one eye of each of 6 New Zealand White rabbits and the eye was held closed for one second. The responses were scored 24, 48 and 72 hours after application. After 24 hours, slight swelling and redness of the conjunctiva occurred, which had subsided after 48 hours (irritation index: 0.67 of a maximum of 4 for swelling in 4 of 6 animals and 0.83 of a maximum of 3 for reddening in 5 of 6 animals) (Dow Chemical Company 1989).

5.4 Allergenic effects

In a so-called Draize test, male guinea pigs were given a single intradermal application of 0.05 ml followed by 9 further intradermal applications of 0.1 ml of a 5% preparation of 1-nitropropane (purity 96.12%) in saline at 2-day intervals. After intradermal challenge with 0.1 ml of a 1% preparation carried out 14 days later, no reaction was found in any of the 10 male guinea pigs (Dow Chemical Company 1989).

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

In a screening study carried out according to OECD Test Guideline 422, groups of 12 female and 12 male Sprague Dawley rats were exposed whole-body to 1-nitropropane concentrations of 0, 24, 48 or 96 ml/m^3 for 6 hours per day on 7 days per week. The animals were mated after 14 days and the females exposed up to gestation day 19 (day 47); the males were treated for 28 days (see Section 5.2). The fertil-

ity index and mating index were 83.3% in the 48 ml/m³ and 96 ml/m³ concentration groups, whereas in the low concentration group of 24 ml/m³ and the control group the fertility index and mating index were 100%. The decrease in fertility was not statistically significant and just within the range of the historical controls of the laboratory (83.3%–100%) (Dow Chemical Company 2004). The NOAEC for fertility in this study was 96 ml/m³, the highest concentration tested.

5.5.2 Developmental toxicity

In the study according to OECD Test Guideline 422 described above, the mean litter size at the high concentration of 96 ml/m³ was 11.9 pups/litter, and thus markedly lower than that in the control group with 14.0/litter. There were no differences between the four exposure groups in the number of dead pups at birth and on days 1 and 4 thereafter. The data for the individual animals showed that in the 96 ml/m³ group three of 10 dams had litters with less than 12 animals (by comparison: controls 1/12, 24 ml/m³ 1/12, 48 ml/m³ 0/10). The effect is not significant, although the incidence does lie outside that of the historical controls of the laboratory. The weights at birth of the male and female offspring in the high concentration group were significantly increased. The weight at birth was inversely related to the litter size and is therefore a secondary effect. The weight at birth of the animals in the control group was lower than that of the historical controls. The authors attribute the smaller litter sizes in the 96 ml/m³ group to maternal toxicity or effects from nasal irritation. There were no treatment-related effects on post-implantation losses, gestation duration, the number of dead and live offspring, survival up to day 4 after birth, or on the ratio of male to female offspring (see Section 5.2.1; Dow Chemical Company 2004). Because of the reduced litter size at the high concentration, the NOAEC for foetotoxicity was 48 ml/m³; malformations were not examined.

5.6 Genotoxicity

In a large number of in vitro studies 1-nitropropane was not found to have mutagenic potential in bacteria with and without the addition of a metabolic activation system or in cultivated rat hepatocytes. The results of a chromosomal aberration test with Chinese hamster lung (CHL) cells was negative. In primary cultures of the rat, mouse and hamster and in human cell cultures, 1-nitropropane did not increase the DNA repair activity (documentation "1-Nitropropane" 1999; Cunningham and Matthews 1991; ECB 2000; ECHA 2015).

The results were positive in an unscheduled DNA synthesis (UDS) test with primary rat hepatocytes at a concentration of 1 μM 1-nitropropane (no other details; Williams et al. 1989).

In a micronucleus test with V79 cells, there was an increase in the induction of micronuclei at concentrations of 3 mM 1-nitropropane and above after incubation for 5 hours. Also, the number of multinucleated cells (presumably apoptotic bodies) determined in parallel was increased. The number of micronuclei did not increase, however, in the H4IIEC3/G, 2sFou and C2rev7 rat liver cell lines after incubation

for 5 hours with up to 10 mM 1-nitropropane. A test for the induction of DNA repair synthesis yielded negative results in all four cell lines (Roscher et al. 1990).

After incubation with concentrations of 0, 0.3, 1, 3 or 10 mM 1-nitropropane (purity 97.4%, main impurity 2.3% 2-nitropropane, no other details) without metabolic activation, there was an increase in TG mutants in a hypoxanthine-guanine phosphoribosyltransferase (HPRT) gene mutation test with V79 cells (ECHA 2015).

In a large number of in vivo tests, 1-nitropropane did not induce micronuclei or DNA repair activity in mice and rats (documentation "1-Nitropropane" 1999; Bingham et al. 2001).

Summary

Overall, the available studies do not provide evidence of genotoxic effects of 1-nitropropane in somatic cells in vitro and in vivo.

5.7 Carcinogenicity

Groups of 125 male and 125 female Long Evans rats were exposed to 1-nitropropane concentrations of 0 or 101 ml/m^3 for up to 21.5 months. Gross-pathological and histopathological examinations of the liver did not reveal abnormal findings. No liver carcinomas were found. Microscopic examination of 25 further organs provided no evidence of treatment-related effects. Detailed data are lacking. By comparison, treatment with 100 ml 2-nitropropane/m^3 for 12 months led to an increase in the incidence of liver carcinomas (documentation "1-Nitropropane" 1999; Griffin et al. 1982).

Gavage administration of 89 mg 1-nitropropane/kg body weight three times per week for 16 weeks and subsequently once a week for 10 weeks did not increase the tumor incidence in 26 male Sprague-Dawley rats even 77 weeks after the start of treatment (documentation "1-Nitropropane" 1999; Fiala et al. 1987).

Daily gavage administration of 1-nitropropane doses of 0, 0.3, 3 or 10 mg/day to groups of 3 female and 3 male F344 rats or to 15 animals of each sex in the middle dose group on 5 days per week for 52 weeks did not produce an increase in tumor incidence. The only unusual finding was a papilloma in the oesophagus of one male animal from the middle dose group (Hadidian et al. 1968).

Summary

Unlike its homologue, 2-nitropropane, 1-nitropropane was not found to be carcinogenic.

6 Manifesto (MAK value/classification)

The critical effect is irritation of the squamous epithelium and the olfactory epithelium in the nose of rats after inhalation of 1-nitropropane.

MAK value. The previous MAK value was based on a human study, according to which volunteers reported eye irritation after exposure for 15 minutes to 1-nitropropane concentrations of 150 ml/m^3 (Silverman et al. 1946). The short exposure

duration is a shortcoming of this study. In the meantime, an inhalation study in rats with repeated exposure has been carried out, which is now used for the derivation of the MAK value.

From a 47-day inhalation study in female rats (Dow Chemical Company 2004), a NOAEC of 24 ml/m³ (≙ 89 mg/m³) was obtained, and from the exposure of male rats for 28 days a NOAEC of 48 ml/m³. This suggests there is an increase in the effects with long-term exposure or a difference in the sensitivity of the sexes. In the higher concentration groups, minimal to slight degeneration and inflammation of the olfactory and squamous epithelium in the nasal cavity were found. The severity and incidence of these effects increased with the exposure concentration (Dow Chemical Company 2004). The systemic NOAEC in both sexes is 48 ml/m³ (177 mg/m³), corresponding to about 50 mg/kg body weight and day (6 hours/day, respiratory volume 0.8 l/min/kg body weight; 100% absorption).

Using the method of Brüning et al. (2014) for the extrapolation of the NOAEC of 24 ml/m³ for effects in the squamous epithelium of female rats (1:3), and assuming a possible increase in the effects with long-term exposure (1:4 instead of 1:6, as the exposure was longer than short-term but shorter than medium-term) and also taking into consideration that the animals were exposed on 7 days per week, compared with 5 days per week at the workplace, a MAK value of 2 ml/m³ is obtained according to the preferred value approach.

Peak limitation. The local effect on the squamous and olfactory epithelium of rats is the critical effect; this is decisive for the derivation of the MAK value. The substance is therefore assigned to Peak Limitation Category I. The MAK value was derived according to the procedure of Brüning et al. (2014) and its aim is to protect against both histopathological changes and sensory irritation of the nasal mucosa. However, the MAK value is considerably lower than the NOAEC obtained in the study with volunteers, according to which 100 ml/m³ was considered tolerable and in which eye irritation occurred at 150 ml/m³, but no irritation in the nose. Although there are considerable methodological uncertainties in the study of Silverman et al. (1946), the NOAEC from this study can nevertheless be used as a rough guide in so far as pronounced sensory irritation is not to be expected in this concentration range. As the MAK value is only 1/75 of this NOAEC for nasal sensory irritation and 1/50 of the NOAEC for eye irritation in the study with volunteers, an excursion factor of 8 appears to be justified in this case, allowing a peak concentration of 16 ml/m³.

Prenatal toxicity. For developmental toxicity there is only a screening study according to OECD Test Guideline 422 available. The NOAEC for foetotoxicity was 48 ml/m³ due to reduced litter sizes at the high concentration of 98 ml/m³.

Due to the absence of teratogenicity studies, 1-nitropropane is assigned to Pregnancy Risk Group D.

Carcinogenicity. As no evidence of carcinogenicity was found in the available studies, 1-nitropropane is not classified in one of the categories for carcinogens.

Germ cell mutagenicity. The available studies yielded no evidence of genotoxic effects of 1-nitropropane in somatic cells in vitro and in vivo. There are no data

available for effects on germ cells. 1-Nitropropane is therefore not classified in one of the categories for germ cell mutagens.

Absorption through the skin. Assuming the exposure of 2000 cm^2 of skin for one hour to undiluted 1-nitropropane, the dermal absorption of 358 mg can be estimated for humans from an in vitro study (Section 3.1). As the NOAEC for systemic effects after short-term inhalation exposure of rats was 48 ml/m^3 (177 mg/m^3), a systemically tolerable amount of 155 mg is obtained after extrapolation to long-term exposure and to humans (177 $mg/m^3 \times 10\ m^3 \times 7/5/4$ (time)/2 (animal/human extrapolation)/2 (increased respiratory volume at the workplace)). Therefore, the amount absorbed through the skin is more than the systemically tolerable amount, so that the substance is designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. As no clinical cases of sensitization to 1-nitropropane are available, and there is merely one negative result from an animal experiment with intradermal application not carried out according to the guidelines, the substance is designated neither with "Sh" (for substances which cause sensitization of the skin) nor with "Sa" (for substances which cause sensitization of the airways).

7 References

Bingham E, Cohrssen B, Powal CH (Eds) (2001) Patty's toxicology, Vol 4, Wiley & Sons, New York, NY, USA, 573–575

Brüning T, Bartsch R, Bolt HM, Desel H, Drexler H, Gundert-Remy U, Hartwig A, Jäckh R, Leibold E, Pallapies D, Rettenmeier AW, Schlüter G, Stropp G, Sucker K, Triebig G, Westphal G, van Thriel C (2014) Sensory irritation as a basis for setting occupational exposure limits. Arch Toxicol 88: 1855–1879

Cunningham ML, Matthews HB (1991) Relationship of hepatocarcinogenicity and hepatocellular proliferation induced by mutagenic noncarcinogens vs carcinogens. 1- vs 2-nitropropane. Toxicol Appl Pharmacol 110: 505–513

Davis RA (1993) Aliphatic nitro, nitrate, and nitrite compounds. in: Clayton GC, Clayton FE (Eds) Patty's industrial hygiene and toxicology, Wiley & Sons, New York, NY, USA, 599–662

Dequidt J, Vasseur P, Potencier J (1972) Experimental toxicologic study of some nitroparaffins: 1-nitropropane. Bull Soc Pharm Lille 2: 131–136

Dow Chemical Company (1974) Testing of materials for eye irritation in rabbits. Substances labelled nitromethane, nitroethane, and 2-nitropropane. Altech Laboratories INC., Dow Chemical Company, Midland, MI, USA, unpublished report

Dow Chemical Company (1981) Summary of acute toxicity profile of 1-nitropropane. Toxicology & Environmental Research and Consulting, ID: PLR-182, Dow Chemical Company, Midland, MI, USA, unpublished report

Dow Chemical Company (1989) Primary eye irritation study of 1-nitropropane in New Zealand White rabbits. Toxicology & Environmental research and Consulting, ID: K-004599-003, Dow Chemical Company, Midland, MI, USA, unpublished report

Dow Chemical Company (1996) 1-Nitropropane: Twenty-eight day subacute oral (gavage) toxicity study in the rat. Safepharm Laboratories Limited, Angus Chemical Company, Buffalo Grove, IL, USA, Dow Chemical Company, Midland, MI, USA, unpublished report

Dow Chemical Company (2004) 1-Nitropropane: a combined repeated inhalation exposure study with the reproduction/developmental toxicity screening test in CD rats. Toxicology & Environmental Research and Consulting, ID 021127, Dow Chemical Company, Midland, MI, USA, unpublished report

ECB (European Chemicals Bureau) (2000) 1-Nitropropane. IUCLID dataset, 18.02.2000, ECB, Ispra, Italy

ECHA (European Chemicals Agency) (2015) Information on registered substances. Dataset on 1-nitropropane (CAS Number 108-03-2), joint submission, first publication 03.03.2011, last modification 24.12.2015,
http://echa.europa.eu/web/guest/information-on-chemicals

Fasano WJ, McDougal JN (2008) In vitro dermal absorption rate testing of certain chemicals of interest to the Occupational Safety and Health Administration: summary and evaluation of USEPA's mandated testing. Regul Toxicol Pharmacol 51: 181–194

Fiala ES, Czerniak R, Castonguay A, Conaway CC, Rivenson A (1987) Assay of 1-nitropropane, 2-nitropropane, 1-azoxypropane and 2-azoxypropane for carcinogenicity by gavage in Sprague-Dawley rats. Carcinogenesis 8: 1947–1949

Fiserova-Bergerova V, Pierce JT, Droz PO (1990) Dermal absorption potential of industrial chemicals: criteria for skin notation. Am J Ind Med 17: 617–635

Frederick CB, Michele L, Bush ML, Lomax LG, Kurt A, Black KA, Finch L, Kimbell JS, Morgan KT, Ravi P, Subramaniam RP, Morris JB, Ultman JS (1998) Application of a hybrid computational fluid dynamics and physiologically based inhalation model for interspecies dosimetry extrapolation of acidic vapors in the upper airways. Toxicol Appl Pharmacol 152: 211–231

Griffin TB, Stein AA, Coulston F (1982) Inhalation exposure of rats to vapors of 1-nitropropane at 100 ppm. Ecotoxicol Environ Saf 6: 268–282

Guy RH, Potts RO (1993) Penetration of industrial chemicals across the skin: a predictive model. Am J Ind Med 23: 711–719

Haas-Jobelius M, Korte F, Coulston F (1989) Disposition and metabolism of 1-nitropropane in rats and chimpanzees. Biomed Environ Sci 2: 249–264

Haas-Jobelius M, Coulston F, Korte F (1992) Effects of short term inhalation exposure to 1-nitropropane and 2-nitropropane on rat liver enzymes. Ecotoxicol Environ Saf 23: 253–259

Hadidian Z, Fredrickson N, Weisburger EK, Weisburger JH, Glass RM, Mantel N (1968) Tests for chemical carcinogens. Report on the activity of derivatives of aromatic amines, nitrosamines, quinolines, nitroalkanes, amides, epoxides, aziridines, and purine antimetabolites. J Natl Cancer lnst 41: 985–1036

Lai DY, Woo Y, Arcos JC, Argus MF (1982) Nitroalkanes and nitroalkenes. Carcinogenicity and structure activity, relationships, other biological properties, metabolism, environmental significance. Current Awareness Program Vol. III, Preparation for the Chemical Hazard Identification Branch "Current Awareness" Program: 1–19,
http://nepis.epa.gov/exe/ZyPDF.cgi/91014SX0.PDF?Dockey=91014SX0.PDF

Linhart I, Gescher A, Goodwin B (1991) Investigation of the chemical basis of nitroalkane toxicity: tautomerism and decomposition of propane 1- and 2-nitronate under physiological conditions. Chem Biol Interact 80: 187–201

Machle W, Scott EW, Treon J (1940) The physiological response of animals to some simple mononitroparaffins and to certain derivatives of these compounds. J Ind hyg Toxicol 22: 315–332

NIOSH (National Institute for Occupational Safety and Health) (2003) Propane, 1-nitro-, registry of toxic effects of chemical substances (RTECS), Databank excerpt, NIOSH, Cincinnati, OH, USA

NLM (National Library of Medicine) (2006) 1-Nitropropane. Hazardous Substances Data Bank, http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

NTP (National Toxicology Program) (2014) Toxicity effects. CAS registry Number: 108-02-3. Testing status of agents at NTP, US Department of Health and Human Services, National Institutes of Health, Bethesda, MD, USA

Roscher E, Ziegler-Skylakakis K, Andrae U (1990) Involvement of different pathways in the genotoxicity of nitropropanes in cultured mammalian cells. Mutagenesis 5: 375–380

Silverman L, Schulte HF, First MW (1946) Further studies on sensory response to certain individual solvent vapors. J Ind hyg Toxicol 28: 262–266

Stokinger HE (1982) Aliphatic nitro compounds, nitrates, nitrites. in: Clayton GC, Clayton FE (Eds) Patty's industrial hygiene and toxicology, Vol 2c, Wiley & Sons, New York, NY, USA, 4141–4208

Ullrich V, Hermann G, Weber P (1978) Nitrite formation from 2-nitropropane by microsomal monooxygenase. Biochem Pharmacol 27: 2301–2304

Williams GM, Mori H, McQueen CA (1989) Structure-activity relationships in the rat hepatocyte DNA-repair test for 300 chemicals. Mutat Res 221: 263–286

Wilschut A, ten Berge WF, Robinson PJ, McKone TE (1995) Estimating skin permeation. The validation of five mathematical skin permeation models. Chemosphere 30: 1275–1296

Zitting A (1988) Nitroalkanes. in: Heimbürger G, Lundberg P (Eds) Criteria Documents from the Nordic Expert Group. Arbete och Hälsa 33, Solna, Schweden, 115–163, https://gupea.ub.gu.se/bitstream/2077/4078/1/ah1988_33.pdf

completed February 24, 2016