Nitroethane

(CAS No: 79-24-3)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

No. 2000/15OSH/124, The Hague, June 8, 2004

Preferred citation:
Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. Nitroethane; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2004; 2000/15OSH/124.

all rights reserved

1 Introduction

The present document contains the assessment of the health hazard of nitroethane by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by A Spooren, Ph.D. and H Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of nitroethane has been based on the review by the American Conference of Governmental Industrial Hygienists (ACGIH) (ACG91). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, in February 1998, literature was searched in the on-line databases Medline, Toxline, and Chemical Abstracts, starting from 1966, 1965, and 1967, respectively, and using the following key words: 79-24-3 and nitroethane.

In July 2000, the President of the Health Council released a draft of the document for public review. No comments were received.

An additional search in Toxline and Medline in November 2003 did not result in information changing the committee's conclusions.

2 Identity

name	:	nitroethane
synonyms	:	ethane, nitro-
molecular formula	:	$C_2H_5NO_2$
structural formula	:	CH_3-CH_2NO_2
CAS number	:	79-24-3

3 Physical and chemical properties

molecular weight	:	75.07
boiling point	:	114°C
melting point	:	-90°C
flash point	:	28, 31°C (closed cup); 41°C (open cup)
vapour pressure	:	at 25°C: 2.9 kPa
solubility in water	:	slightly soluble (at 20°C: 4.5 mL/100 mL)
log $P_{octanol/water}$	:	0.18 (experimental); 0.45 (calculated)
conversion factors	:	at 20°C, 101,3 kPa: 1 ppm = 3.1 mg/m^3 1 mg/m^3 = 0.32 ppm

Data from ACG91, NLM03, http://esc.syrres.com.

Nitroethane is an oily, colourless liquid with a somewhat pleasant odour (fruity aroma). An odour threshold of 2.1 ppm (6.5 mg/m^3) has been reported (Amo83).

4 Uses

Nitroethane is used as a propellant gas in spray cans and as a solvent for cellulose esters, vinyl, alkyd, and other resins and waxes. It is also used in chemical syntheses (ACG91).

5 Biotransformation and kinetics

The committee did not find human data on the biotransformation and kinetics of nitroethane.

In anaesthetised male F344 rats, 58% of inhaled nitroethane was absorbed by the respiratory tract at a concentration of 1000 ppm (3100 mg/m^3) and a respiratory minute volume of 53 mL/min. Using isolated upper and lower respiratory tracts and flow rates equivalent to the animals' minute volume of 53 mL/min, absorption percentages were 65 and 71%, respectively. Using a flow rate equivalent to a minute volume of 105 mL/min, absorption by the isolated upper respiratory tract decreased to ca. 53%. The absorption by the isolated upper respiratory tract was linear over a 10-fold exposure range of 100 to 1000 ppm (310-3100 mg/m^3) (Sto84). Applications to the skin gave no evidence of absorption sufficiently high to result in systemic injury (concentration unknown) (Mac40).

Thirty hours following intravenous (ca. 0.3 g/kg bw) or oral (1 or 2 g/kg bw) administration to rabbits, almost none nitroethane could be recovered. Nitroethane was partly excreted via the lungs (Mac42).

By either inhalation or oral administration, nitroethane was shown to be metabolised to aldehyde and nitrite, with the latter product eventually oxidised to nitrate (Sco43).

In vitro, oxidative denitrification of nitroalkanes has been shown to occur by two mechanisms: the microsomal cytochrome P450 monooxygenase system and various flavoenzyme oxidases (Dav93).

6 Effects and mechanism of action

Human data

There are several case reports on nitroethane producing methaemoglobinaemia in young children (13- to 27-month old) after ingesting nitroethane-containing artificial nail-removing products (Hor94, Ost95, She98, Wel96).

No further human data were available.

Animal data

Irritation and sensitisation

Exposure of rabbits and guinea pigs to 500 ppm (1555 mg/m^3) nitroethane caused respiratory tract and conjunctival irritation; eyelids were reddened, discharges appeared, and the eyes were kept closed. No evidence of skin irritation was found after 4-hour skin application for 5 days (concentration unknown) (Mac40).

The committee did not find data from sensitisation studies of nitroethane.

Acute toxicity

Referring to a chemical company's data sheet, ACGIH stated that rats exposed to 13,000 ppm (40,430 mg/m^3) nitroethane for 6 to 7 hours all died while no effects were observed following exposure to 2200 ppm (6842 mg/m^3) for 6 hours (ACG91).

When rabbits and guinea pigs (n=2/group) were exposed to nitroethane at 500-30,000 ppm (1555-93,300 mg/m^3) for durations ranging from 0.5 hour to a total of 140 hours (given as daily 6-hour exposures), a dose-related mortality was observed. Rabbits and guinea pigs survived exposures to 2500 ppm (7775 mg/m^3) for 3 hours or 1000 ppm (3110 mg/m^3) for 6 hours, but exposure to 1000 ppm (3110 mg/m^3) for 12 hours or 30,000 ppm for 30 minutes resulted in the death of 1 out of 2 rabbits. Rabbits exposed to 5000 ppm (15,550 mg/m^3) for 3 hours died, and autopsy revealed liver damage. The morphological liver damage was attributed to peroxidation. Nitroethane also exhibited anaesthetic properties (narcosis) in animals exposed to 30,000 ppm for longer than 1 hour or to 1000 ppm (3110 mg/m^3) for 5 or 6 hours. At 500 ppm, the lowest concentration used

in this study, the animals survived an extended exposure period of 140 hours (Mac40).

Rats (strain, number, sex not specified) exposed to 13,000 ppm (40,430 mg/m^3) died within the course of the experiment within 6 to 7 hours. Methaemoglobin levels were 2.8%. No mortality occurred following 5 subsequent 6-hour exposures to 2200 ppm (6842 mg/m^3). No methaemoglobinaemia was found in these animals (Deq72).

In rats, an oral LD_{50} of 1100 mg/kg bw has been reported (NIO03, Ric94). For mice, oral LD_{50}s were 860 (NIO03, Ric94) and approximately 2260 mg/kg bw (Hit79). Amounts between 500-750 mg/kg bw were lethal to rabbits (Mac40).

Male 3-month-old rats (n=5) dosed intraperitoneally with 200 mg/kg bw of nitroethane showed minor liver damage which was attributed to limited peroxidative damage possibly involving reduction of the nitro group (Zit82). One intraperitoneal dose of 1.6 g/kg bw or 14 daily doses of 0.11 g/kg bw administered over 20 days induced very low methaemoglobin levels in rats (Deq72).

Repeated-dose toxicity including carcinogenicity

In a study carried out to determine exposure concentrations for a 13-week study, rats (F344) and mice ($B6C3F_1$) (n=5/species/sex/group) were exposed to analytical concentrations of 0, 350, 1000, 2000, or 4000 ppm (0, 1000, 3000, 6000, 12,000 mg/m^3), 6 hours/day, for 4 days. During the daily exposures, the control animals were not housed in the inhalation chambers but in similar cages in the animal room. In rats, all animals of the highest concentration group died after 2 exposures, showing symptoms of anaesthesia, poor coordination, slow laboured respiration, and dull dark-red eyes with some exudate around them. Gross post-mortem examination revealed a dark cyanotic appearance to the extremities and thymic atrophy in some rats. Exposure to 2000 ppm caused drowsiness (only after the first exposure), dull dark-red eyes, signs of eye and nasal irritation, rough coats, and body weight loss. At autopsy, hyperaemia and thymic atrophy were seen in some of the rats. In the animals exposed to 1000 ppm, drowsiness (only after the first exposure), dull dark-red eyes, and signs of nasal irritation were observed. The first exposure caused body weight loss, but the animals gained weight after subsequent exposures. Upon gross post-mortem examination, there was thymic atrophy in some animals. Apart from thymic atrophy, no effects were found after exposure to 350 ppm. In mice, apart from occasional thymic atrophy, no effects were seen in the animals exposed to 350

and 1000 ppm. Exposure to 2000 ppm caused slightly laboured respiration (after the first exposure only), drowsiness, and slight incoordination, while 1 male and 1 female animal died after 3 exposures. Gross pathological changes were thymic atrophy, decreased adipose tissue, bile or haemolysed blood in the stomach and/or small intestine, and decreased ingesta in the gastrointestinal tract. These changes were also seen in the animals exposed to 4000 ppm. All animals of this exposure group died before the third exposure (Gus82a).

In a 90-day inhalation study* rats (F344) and mice ($B6C3F_1$) (n=15/species/sex/group) were exposed to 0, 100, 350, or 1000 ppm (310, 1090, or 3110 mg/m^3) nitroethane, 6 hours/day, 5 days/week. During the exposure days, control animals were placed in an identical exposure chamber as the treated animals. Animals were sacrificed after 29-30 (interim kills; 5/species/sex/group) and 92-93 days. Haematology (including Heinz bodies and methaemoglobin), clinical chemistry, and urinalysis parameters were determined. Body and organ (liver, kidneys, brain, heart, thymus, testes) weights were obtained, and gross and microscopic examinations were performed. In rats, treatment did not induce mortality. Generally, exposure to nitroethane caused an oxidative stress on the haemoglobin of the treated animals that resulted in the most remarkable effect, viz, methaemoglobinaemia. In the high-concentration animals, this was detected by direct measurement and manifested by clinical signs such as dull, dark-red eyes and greyish or bluish skin of the extremities (cyanosis). Other effects such as a premature release of bone marrow reticulocytes, splenic extramedullary haematopoiesis, and increased presence of Heinz bodies were thought to be the consequence of the oxidative stress and methaemoglobinaemia as well. In addition, exposure to 1000 ppm caused decreased body weight gain (with secondary effects on other parameters), moderate degenerative and inflammatory changes in the olfactory nasal epithelium, slight hepatocellular vacuolisation, splenic congestion, slightly decreased cytoplasmic granularity of the ductal epithelial cells of the salivary glands, and slightly decreased cytoplasmic granularity of the renal cortical tubular epithelium. In the 350-ppm group, similar but less severe changes in methaemoglobin level, body weight (gain), spleen, liver, nasal turbinates, and salivary glands were found. In animals exposed to 100 ppm, only minimal or very slight changes were found in methaemoglobin level, spleen, and salivary glands. In mice, changes were generally similar but less severe than those found in rats. Four male animals died during the study (1 control, 2 exposed to 350 ppm, 1 exposed to 1000 ppm), but their death was not considered to be treatment related. In the 1000-ppm group, there were increased

* No tables were present in the copy of the study report available to the committee.

methaemoglobin levels with an increased presence of reticulocytes and Heinz bodies, moderate degeneration of the olfactory mucosa with or without inflammation including moderate glandular hyperplasia, slightly increased cytoplasmic homogeneity of the liver, transient salivary gland alterations of decreased cytoplasmic granularity and decreased eosinophilic staining, and presence of multinucleated spermatids in the testes. In the 350-ppm group, only changes in methaemoglobin level, liver, and nasal turbinates were found. In the 100-ppm group, effects were limited to minimal changes in the nasal turbinates in females only and to transient effects (found at the interim and not at the terminal kill) on salivary glands (Gus82a, Gus82b). From this study, no NOAEL can be derived since effects were observed at all concentrations tested. For both rats and mice, 100 ppm (310 mg/m^3) is concluded to be the LOAEL. The (occasional, rather consistently found) thymus effects reported in the range-finding study were obviously not very important. In the 13-week study, no such effects were reported in mice. As to rats, the only observation reported was a decreased thymus size in a few animals of the high-concentration group at the terminal kill without microscopic changes.

Male and female Long-Evans rats (n=40/sex/group) were exposed by inhalation to 100 or 200 ppm (310 or 620 mg/m^3) nitroethane, 7 hours/day, 5 days/week, for 2 years. Control groups (n=40/sex) were included, but not housed in the exposure chamber during the exposure periods. All animals sacrificed were examined grossly and histologically. Many organs and tissue were prepared for microscopic examination; of the respiratory tract, the lungs and the trachea were included but not the nasal cavity. Blood samples were also obtained from representative groups of animals (10 males and 10 females) for haematology (erythrocyte counts, leukocyte counts, mean corpuscular volume, packed cell volume, and haemoglobin; methaemoglobin was not included) and serum chemistry studies (aspartate aminotransferase, alanine aminotransferase, total bilirubin, total protein, blood urea nitrogen, creatine, sodium, and potassium). There was no treatment-related mortality. Mean terminal body weights were decreased in both treatment groups (by 5-6% in males, 12-13% in females) when compared to those in controls. It was stated that upon statistical analysis of the results of the male groups, there was a significant decrease in mean body weights in the 100-ppm group throughout the study and in the 200-ppm group during weeks 6-15 and thereafter occasionally. As to females, the differences were significant in the 200-ppm group throughout the study and in the 100-ppm group occasionally only. There were no treatment-related increases in the incidence of any tumour. The treatment did not induce any other effect on any of the parameters investigated in any of the treated groups (Gri86). From this study,

100 ppm (310 mg/m^3), the lowest level tested, is considered to be the LOAEL since 2-year exposure to this concentration induced a slight effect on male body weight.

No statistically significant increase in the incidence of any tumour was found in rats (Long-Evans hooded) exposed intermittently to approximately 9 ppm nitroethane and 9-27 ppm diethylhydroxylamine and continuously to an unknown concentration of diethylamine hydrogen sulphite, for about 29 months, when compared with controls (Hei81). When mice (ICR Swiss) were exposed to about 10 ppm nitroethane and 10 ppm diethylhydroxylamine, 6-8 hours/day, 5 days/week, and to an unknown concentration of diethylamine hydrogen sulphite, 24 hours/day, 7 days/week, for over 2 years, a decrease in the incidence of all tumours was found in the female animals when compared with controls. In males, exposure induced a marginally statistically significant increase (P=0.048) in the incidence of subcutaneous tumours (principally fibrosarcomas) (Hei82).

Mutagenicity and genotoxicity

Nitroethane was not mutagenic in *S. typhimurium* strains TA92, TA98, TA100, TA102, TA1535, TA1537, and TA1538 when tested with and without metabolic activation (Day89, Dom80, Hit79, Löf86, War88).

In vivo, nitroethane was also negative in the micronucleus test with mice given 2 consecutive daily oral doses of nitroethane of 282, 565, or 1130 mg/kg bw. The doses were selected based on an oral LD_{50} of about 2260 mg/kg bw (Hit79). The committee considers this study inadequate. No data were presented to evaluate whether the doses were high enough or whether the compound has reached the bone marrow. Furthermore, animals were sacrificed 6 hours after the last dose, while according to current OECD and EU guidelines, in case of multiple dosing, samples should be taken once between 18 and 24 hours following the final treatment for bone marrow and once between 36 and 48 hours following the final treatment for the peripheral blood.

A negative result was reported in a dominant lethal test in which male rats were exposed to 10 ppm nitroethane and 9 ppm diethylhydroxylamine for several months (1541-1673 hours) and mated with unexposed virgin females (two females per male) (Leg79). However, in view of the low concentration tested, the committee considers this study inadequate.

Reproduction toxicity

Mice exposed to 1000 ppm (3110 mg/m^3) nitroethane showed multinucleated spermatids in the testes, an effect indicating chromosomal damage (Gus82a, Gus82b).

There is no information available on the development or reproduction toxicity potential in mammals exposed to nitroethane only. However, neither maternal nor developmental effects were observed in a teratology study in which pregnant mice (ICR Swiss; n=25) were exposed to approximately 14 ppm nitroethane and approximately 9 ppm diethylhydroxylamine, 6-8 hours/day, and to an unknown concentration of diethylamine hydrogen sulphite, 24 hours/day, from gestational day 6 to 17 (Bel78). In a 3-generation reproduction toxicity study, no statistically significant differences regarding parental and reproduction toxicity parameters were found between control mice and mice (ICR Swiss) exposed to approximately 11 ppm nitroethane and approximately 8 ppm diethanolhydroxylamine, 6-8 hours/day, 5 days/week, and to an unknown concentration of diethylamine hydrogen sulphite, 24 hours/day, 7 days/week (Hei79).

7 Existing guidelines

The current administrative occupationally exposure limit (MAC) for nitroethane in the Netherlands is 60 mg/m^3 (20 ppm), 8-hour TWA.

Existing occupational exposure limits for nitroethane in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

The committee did not find data on occupationally exposed workers. Case reports on poisoning episodes following accidental ingestion indicate that nitroethane can produce methaemoglobinaemia in humans.

There are no data on the potential irritation or sensitisation from experiments meeting current criteria. However, limited data from old inhalation exposure experiments showed that nitroethane might be a respiratory tract and eye irritant in rabbits and guinea pigs.

The committee considers methaemoglobinaemia to be the critical effect in rats and mice following repeated inhalation exposure to nitroethane. Furthermore, there were effects on body weight, spleen, liver, salivary glands, and nasal turbinates.

There was no evidence for carcinogenicity in a 2-year inhalation study in rats at concentrations (viz., 100 and 200 ppm) that caused slight effects on body weight only.

Nitroethane was negative in mutagenicity tests in *S. typhimurium* strains TA92, TA98, TA100, TA102, and TA1537 with and without metabolic activation. Nitroethane caused an increase in multinucleated spermatids in mice exposed to 1000 ppm (3110 mg/m^3) for 13 weeks, but not in mice exposed to 350 ppm (1090 mg/m^3). Because of flaws in design, the committee considered an *in vivo* micronucleus test in mice and a dominant lethal test in rats (both with a negative result) as inadequate.

Developmental and parental parameters were not affected when nitroethane was tested in a teratology and 3-generation reproduction toxicity study with mice at a concentration of approximately 10 ppm in the presence of vapours of diethylhydroxylamine and diethylamine hydrogen sulphite.

Since methaemoglobinaemia was the critical effect observed in the 13-week study by Gushow et al. at levels below those inducing effects on body weight (gain) and since this was not addressed in the 2-year study (in which effects on body weight were critical), the committee takes the 13-week inhalation study as a starting point in deriving a health-based recommended occupational exposure limit (HBROEL). In this study, nitroethane induced besides methaemoglobinaemia, decreased body weight (gain) and histological lesions of the nasal turbinates, liver, spleen, kidneys, and salivary glands. Generally, effects occurred in both rats and mice, but mice were less sensitive. A NOAEL could not be derived since at the lowest level tested minimal or very slight changes were found in methaemoglobin levels, spleen, and salivary glands in rats and in the nasal turbinates (in females only) and salivary glands (in interim kills only) in mice. Thus, the LOAEL of 310 mg/m^3 (100 ppm) is taken as a starting point. For the extrapolation to an HBROEL, an overall assessment factor of 18 is established. This factor covers the following aspects: the absence of a NOAEL and inter- and intraspecies variation. Thus, applying this factor and the preferred-value approach, a health-based occupational exposure limit of 20 mg/m^3 is recommended for nitroethane.

The committee recommends a health-based occupational exposure limit for nitroethane of 20 mg/m^3 (6 ppm), as an 8-hour time-weighted average concentration.

References

ACG91 American Conference of Governmental Industrial Hygienists (ACGIH). Nitroethane. In: Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati OH, USA; ACGIH®, 1991: 1105-6.

ACG03 American Conference of Governmental Industrial Hygienists (ACGIH). Guide to occupational exposure values - 2003. Cincinnati OH, USA: ACGIH®, 2003: 96.

ACG04 American Conference of Governmental Industrial Hygienists (ACGIH). 2004 TLVs® and BEIs® based on the documentation of the Threshold Limit Values for chemical substances and physical agents & Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, 2004: 42.

Amo83 Amoore JE, Hautala E. Odor as an aid to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. J Appl Toxicol 1983; 3: 272-90.

Arb02 Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2002: 33 (At-vejledning C.0.1).

Bel78 Beliles RP, Makris SL, Ferguson F, et al. Teratology study in mice subjected to inhalation of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1978; 17: 165-76.

Dav93 Davis RA. Aliphatic nitro, nitrate, and nitrite compounds. In: Clayton GD, Clayton FE, eds. Toxicology. 4th ed. New York, USA: John Wiley & Sons, 1993:599-662. (Patty's industrial hygiene and toxicology; Vol II, Pt A).

Day89 Dayal R, Grescher A, Harpur ES, et al. Comparison of the hepatoxicity in mice and the mutagenicity of three nitroalkanes. Fundam Appl Toxicol 1989;13: 341-8.

Deq72 Dequidt PJ, Vasseur P, Potencier J. Étude toxicologique expérimentale de quelques nitroparaffines. 3) Étude du nitro-éthane. Bull Soc Pharm Lillie 1972; 4: 137-41.

DFG03 Deutsche Forschungsgemeinschaft (DFG): Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. List of MAK and BAT values 2003. Maximum concentrations and Biological Tolerance Values at the workplace Weinheim, FRG: Wiley-VCH Verlag GmbH & Co. KGaA, 2003: 86 (rep no 39).

Dom80 Domoradzki JY. Evaluation of chlorothene VG and its components in the Ames' Salmonella/ mammalian microsome mutagenicity assay. Midland MI, USA: Dow Chemical, Health Environ Sci, Toxicol Res Lab, 1980; available from NTIS, Springfield VA, USA; order no NTIS/OTS0520701.

EC04 European Commission: Directorate General of Employment and Social Affairs. Occupational exposure limits (OELs); http://europe.eu.int/comm/employment_social/health_safety/areas/ oels_en.htm.

Gri88 Griffin TB, Stein AA, Coulston F. Chronic inhalation exposure of rats to vapors of nitroethane. Ecotoxicol Environ Saf 1988; 16: 11-24.

Gus82a Gushow TS, Bell TJ, Burek JD, et al. Nitroethane: a 4-day and 13-week inhalation study in rats and mice. Midland MI, USA: Dow Chemical, Health Environ Sci, Toxicol Res Lab, 1982; available from NTIS, Springfield VA, USA; order no NTIS/OTS0520703.

Gus82b Gushow TS, Bell TJ, Burek JD, et al. Nitroethane: a 13-week inhalation toxicity study in rats and mice. Toxicologist 1982; 2: 561.

Hei79 Heicklen J, Partymiller K, Kelly N, et al. Three-generation reproduction study in mice subjected to inhalation of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1979; 20: 450-4.

Hei81 Heicklen J, Meagher JF, Weaver J, et al. Toxicological testing of rats subjected to inhalation of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1981; 26: 258-73.

Hei82 Heicklen J, Lundgard R, Partymiller K. Chronic inhalation study of mice subjected to diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1982; 27: 277-89.

Hit79 Hite M, Skeggs H. Mutagenic evaluation of nitroparaffins in the Salmonella Typhimurium/ mammalian microsome test and the micronucleus test. Environ Mutagen 1979; 1: 383-9.

Hor94 Hornfeldt CS, Rabe WH III. Nitroethane poisoning from an artificial fingernail remover. Clin Toxicol 1994; 32: 321-4.

HSE02 Health and Safety Executive (HSE). EH40/2002. Occupational Exposure Limits 2002. Sudbury (Suffolk), England: HSE Books, 2002: 22.

Leg79 Legator M, Kouri RE, Parmar AS, et al. Mutagenic testing of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1979; 20: 99-124.

Löf86 Löfroth G, Nilsson L, Andersen JR. Structure-activity relationship of nitroalkane-induced mutagenicity in the Ames Salmonella assay. Prog Clin Biol Res 1986; 209B: 149-55.

Mac40 Machle W, Scott EW, Treon J. The physiological response of animals to some simple mononitroparaffins and to certain derivatives of these compounds. J Ind Hyg Toxicol 1940; 28: 315-32.

Mac42 Machle W, Scott EW, Treon J. The metabolism of mononitroparaffins. I. Recovery of nitroethane from the animal organism. J Ind Hyg Toxicol 1942; 24: 5-9.

NIO03 US National Institute for Occupational Safety and Health, ed. Ethane, nitro-. In: The Registry of Toxic Effects of Chemical Substances (RTECS) (last update nitroethane file: October 2002); http://www.cdc.gov/niosh.

NLM03 US National Library of Medicine (NLM), ed. Nitroethane. In: The Hazardous Substances Data Bank (HSDB) (last revision date nitroethane file: November 2002; last review date: March 1994); http://toxnet.nlm.nih.gov.

Ost95 Osterhoudt KC, Wiley CC, Dudley R, et al. Rebound severe methemoglobinemia from ingestion of a nitroethane artificial-fingernail remover. J Pediatr 1995; 126: 819-21.

Ric94 Richardson ML, Gangolli S, eds. N107 Nitroethane. In: The dictionary of substances and their effects. Cambridge, UK: Royal Society of Chemistry 1994: 157-9 (Vol 6).

Sco43 Scott WE. The metabolism of mononitroparaffins. III The concentration of nitroethane, nitrite and nitrate in the blood of rabbits during exposure by inhalation and oral administration. J Ind Hyg Toxicol 1943; 256: 20-5.

She98 Shepherd G, Grover J, Klein-Schwartz W. Prolonged formation of methemoglobin following nitroethane ingestion. Clin Toxicol 1998; 36: 613-6.

Sto84 Stott WT, McKenna MJ. The comparative absorption and excretion of chemical vapors by the upper, lower, and intact respiratory tract of rats. Fundam Appl Toxicol 1984; 4: 594-602.

Swe00 Swedish National Board of Occupational Safety and Health. Occupational exposure limit values and measures against air contaminants. Solna, Sweden: National Board of Occupational Safety and Health, 2000: 62 (Ordinance AFS 2000:3).

SZW04 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2004. The Hague, the Netherlands: Sdu Uitgevers, 2004: 36.

TRG03 TRGS 900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArBl 2003; (9).

War88 Warner JR, Hughes TJ, Claxton LD. Mutagenicity of 16 volatile organic chemicals in a vaporization technique with Salmonella typhimurium TA100. Envrion Mutgen 1988; 11 (suppl 11): 111-2.

Wel96 Wells SR, Anderson DA. Severe methemoglobinemia following nitroethane ingestion. J Toxicol Cutaneous Toxicol 1996; 34: 554.

Zit82 Zitting A, Nickels J, Savoleinen H. Comparison of acute toxic effects of intraperitoneally injected nitromethane and nitroethane in rats. Toxicol Lett 1982; 13: 189-94.

Annex

Occupational exposure limits for nitroethane in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	20	60	8 h	administrative		SZW04
Germany						
- AGS	100	310	8 h			TRG03
- DFG MAK-Kommission	100	310	8 h			DFG03
	400	1240	15 min[c]		[d]	
Great-Britain						
- HSE	100	312	8 h	OES		HSE02
Sweden	20	60	8 h			Swe00
	50	150	15 min			
Denmark	100	310	8 h			Arb02
USA						
- ACGIH	100	-	8 h	TLV		ACG04
- OSHA	100	310	8 h	PEL		ACG03
- NIOSH	100	310	10 h	REL		ACG03
European Union						
- SCOEL	-	-				EC04

[a] S = skin notation; which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Maximum number per shift: 4, with a minimum interval between peaks of 1 hour.

[d] Listed among compounds with MAK values but no pregnancy risk group classification.