The MAK Collection for Occupational Health and Safety

2-Methoxypropanol-1

MAK Value Documentation, addendum – Translation of the German version from 2018

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: 2-methoxypropanol-1; maximum workplace concentration; MAK value; peak limitation; irritation; teratogenicity; developmental toxicity; skin absorption

Citation Note: Hartwig A, MAK Commission. 2-Methoxypropanol-1. MAK Value Documentation, addendum – Translation of the German version from 2018. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2019 Apr;4(2):437-450]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2025. https://doi.org/10.34865/mb158947e6519_w

Republished (online): 08 Aug 2025

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.mb158947e6519

Manuscript completed: 22 Mar 2017

Published (online): 25 Apr 2019

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

2-Methoxypropanol-1[1)]/ 2-Methoxypropan-1-ol

MAK Value Documentation

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

DOI: 10.1002/3527600418.mb158947e6519

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 2-methoxypropanol-1 [1589-47-5]. Available publications and unpublished study reports are described in detail.
Critical effects of 2-methoxypropanol-1 are its irritancy and teratogenicity. A MAK value of 5 ml/m³ had been set. By analogy with 2-methoxypropylacetate-1, this value is now reaffirmed. Also, by analogy with 2-methoxypropylacetate-1 Peak Limitation Category I with excursion factor of 2 is set. 2-Methoxypropanol-1 remains assigned to Pregnancy Risk Group B and also remains designated with an "H" (for substances that can be absorbed through the skin in toxicologically relevant amounts).

Keywords

propylene glycol 2-methyl ether; 2-methoxy-1-hydroxypropane; 2-methoxypropan-1-ol; 2-methoxypropanol; 2-methoxy-1-propanol; mechanism of action; toxicokinetics; metabolism; (sub) acute toxicity; (sub)chronic toxicity; irritation; 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

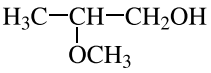
* Email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

1) MAK value applies for the sum of the concentrations of 2-methoxypropanol-1 and its acetate in the air.

2-Methoxypropanol-1[1)]

[1589-47-5]

Supplement 2018

MAK value (2001)	**5 ml/m³ (ppm) ≙ 19 mg/m³**
Peak limitation (2017)	**Category I, excursion factor 2**
Absorption through the skin (2000)	**H**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (1988)	**Pregnancy Risk Group B**
Germ cell mutagenicity	**–**
BAT value	**–**
Synonyms	2-methoxy-1-hydroxypropane 2-methoxypropan-1-ol 2-methoxypropanol propylene glycol 2-methyl ether
Chemical name	2-methoxy-1-propanol
Structural formula	
Molecular formula	$C_4H_{10}O_2$
Molar mass	90.12 g/mol
Melting point	< –50 °C (BUA 1996)
Boiling point at 1013 hPa	130 °C (SRC 2016)
Density at 20 °C	0.938 g/cm³ (NLM 2016)
Vapour pressure at 25 °C	10.97 hPa (SRC 2016)
log K_{OW}[2)]	–0.49 (calculated; SRC 2016)
Solubility at 25 °C	1×10^6 mg/l (calculated; SRC 2016)
1 ml/m³ (ppm) ≙ 3.739 mg/m³	**1 mg/m³ ≙ 0.267 ml/m³ (ppm)**

1) MAK value applies for the sum of the concentrations of 2-methoxypropanol-1 and its acetate in the air.

2) octanol/water partition coefficient.

For 2-methoxypropanol-1, documentation from 1988 (documentation "2-Methoxy-1-propanol" 1990) and supplements from 2000 (supplement "2-Methoxypropanol-1" 2000, available in German only) and 2001 (supplement "2-Methoxypropanol-1" 2001, available in German only) are available.

In 2016, the Commission began using a revised approach for assessing substances with a MAK value based on systemic effects and derived from inhalation studies in animals or studies with volunteers at rest; this new approach takes into account that the respiratory volume at the workplace is higher than under experimental conditions. However, this does not apply to gases or vapour with a blood:air partition coefficient < 5 (see List of MAK and BAT Values, Sections I b and I c). According to the formula of Buist et al. (2012), the blood:air partition coefficient of 2-methoxypropanol-1 is 4104. This supplement evaluates whether the MAK value and the pregnancy risk group of 2-methoxypropanol-1 need to be re-assessed as a result of the higher respiratory volume at the workplace.

1 Toxic Effects and Mode of Action

2-Methoxypropanol-1 was found to be teratogenic in rats and rabbits. In developmental toxicity studies with inhalation exposure, sedation occurred in rats at concentrations of 2000 ml/m^3 and above, and irritation of the respiratory organs at concentrations of 3000 ml/m^3 and above; in rabbits, reduced body weights and retarded body weight gains were found at 539 ml/m^3. After repeated ingestion, reduced haemoglobin levels and slightly reduced erythrocyte counts were found in rats. 2-Methoxypropanol-1 is slightly irritating to the skin and to the eyes. A bacterial mutagenicity test yielded negative results. There are no other data available for the genotoxicity of the substance, or for its carcinogenicity or sensitizing effects.

2 Mechanism of Action

It is assumed that 2-methoxypropionic acid, the main metabolite, is responsible for the developmental toxicity (ECETOC 2005; Hellwig et al. 1994). The mechanism is unknown.

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

Groups of 3 male F344 rats were given single gavage doses of 2-methoxypropanol-1 (^{14}C-labelled at the C-2 position) of 1 or 8.7 mmol/kg body weight (about 90 or 780 mg/kg body weight). The ^{14}C activity in the exhaled air, excreta and tissues was determined, and the metabolites in the urine were isolated and identified. Within 48 hours after administration, about 70% to 80% of the radioactivity was eliminated with the urine, and about 10% to 20% exhaled in the form of $^{14}CO_2$. The amount eliminated with the faeces after 48 hours was 0.8% and 1.6% in the high and low dose

groups, 2.0% and 2.6% was found in the animal carcass, and the recovery was 92.1% and 93.8%, respectively. The highest concentration of radioactivity per gram tissue was found in the blood and the skin after 48 hours, the percentage of the total dose was about 0.5% in the skin, 0.2% in the liver and below 0.05% each in the kidneys, the brain and the testes (Miller et al. 1986).

After the administration of single gavage doses of 2-methoxypropanol-1 of 67.5 or 270 mg/kg body weight to groups of 3 female New Zealand White rabbits, blood samples were taken between 0 and 168 hours later. 2-Methoxypropanol-1 was absorbed very rapidly (T_{max} < 1 h), quickly converted into 2-methoxypropionic acid, and was no longer detectable in the blood 4 to 8 hours after administration. The half-life of 2-methoxypropanol-1 was 0.51 and 0.79 hours, respectively. The half-life of 2-methoxypropionic acid was 37 to 38 hours, the maximum concentration in the blood was attained after 2.5 hours and was 1.1 and 4.2 mM, respectively (Carney et al. 2003).

3.2 Metabolism

After male F344 rats were given single oral doses of ^{14}C-labelled 2-methoxypropanol-1 (see Section 3.1), the main metabolite in the high and low dose groups was 2-methoxypropionic acid, and accounted for 93% and 79% of the radioactivity recovered in the urine, respectively. In addition, a glucuronide metabolite was found at both dose levels, which accounted for 3% to 4% of the radioactivity recovered in the urine (Miller et al. 1986).

As a primary alcohol, 2-methoxypropanol-1 is metabolized mainly to 2-methoxypropionic acid.

4 Effects in Humans

There are no studies in humans available.

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

Groups of 10 male and 10 female Sprague Dawley rats were exposed to 2-methoxypropanol-1 vapour at concentrations of 0 or 6000 mg/m³ for 4 hours. No clinical signs were observed during the 14-day recovery period, and the body weight gains and findings after gross-pathological examination were normal. The 4-hour LC_{50} was > 6000 mg/m³ (BASF AG 1979 b).

5.1.2 Oral administration

Groups of 5 male and 5 female Sprague Dawley rats were given single oral doses of 2-methoxypropanol-1 of 2150 or 5000 mg/kg body weight. Dyspnoea, apathy, unsteady and spastic gait, unkempt fur and poor general condition were observed in the high dose group. Two females in the high dose group died during the first day; they were found to have slightly distended lungs and acute dilation on the right side of the heart with congestive hyperaemia. Gross-pathological examination did not reveal any abnormal findings in the animals killed after 14 days. The oral LD_{50} was therefore > 5000 mg/kg body weight (BASF AG 1979 a).

5.1.3 Dermal application

There are no data available.

5.1.4 Intraperitoneal injection

Groups of 5 male and 5 female NMRI mice were given single intraperitoneal injections of 700 or 2000 mg 2-methoxypropanol-1/kg body weight. In the high dose group, dyspnoea, apathy, unsteady and spastic gait, unkempt fur and poor general condition were observed. There were no deaths. Gross-pathological examination did not reveal any abnormal findings in the animals killed after 14 days. The intraperitoneal LD_{50} was therefore > 2000 mg/kg body weight (BASF AG 1979 a).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

In the developmental toxicity studies with inhalation exposure (see Section 5.5.2), sedation occurred in rats at concentrations of 2000 ml/m^3 and above, and irritation of the respiratory organs at a concentration of 3000 ml/m^3, and in rabbits reduced body weights and retarded body weight gains were observed at a concentration of 539 ml/m^3. No other studies are available.

5.2.2 Oral administration

In a study already described in the documentation of 1988 (documentation "2-Methoxy-1-propanol" 1990), 2-methoxypropanol-1 was administered daily for 10 days by gavage to groups of 5 male Wistar rats in doses of 0 or 1800 mg/kg body weight. In addition, further groups were treated with equimolar doses of 2-ethoxyethanol of 1800 mg/kg body weight or 2-methoxypropylacetate-1 of 2600 mg/kg body weight. Apart from clinical observations, haematological parameters and the organ weights of the testes, thymus, liver, kidneys and spleen were determined at the end of the study. In addition, the testes and thymus were examined histopathologically. While in the animals treated with 2-ethoxyethanol the body, testis and thymus weights were reduced and pronounced atrophy of the thymus and testis were observed at gross pathology, the body and organ weights as well as the gross-pathological findings were

normal in the animals treated with 2-methoxypropanol-1 or 2-methoxypropylacetate-1. The haemoglobin levels, erythrocyte count, haematocrit, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and thrombocyte and leukocyte counts were significantly reduced in the animals treated with 2-ethoxyethanol. The haemoglobin levels (–8%) and erythrocyte count (–5%) were slightly, but significantly reduced in the animals treated with 2-methoxypropanol-1, whereas no significant haematological changes occurred in the animals treated with 2-methoxypropylacetate-1 (BASF AG 1982; Ma-Hock et al. 2005).

5.2.3 Dermal application

There are no data available.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

In a skin irritation study in 6 rabbits with 24-hour occlusive application of undiluted 2-methoxypropanol-1, maximum scores of 2 on a scale up to 4 for erythema on the intact and scarified skin and of 1 for oedema on the intact skin and of 2 on the scarified skin were given. The erythema was reversible after 8 days, and oedema formation after 72 hours. The primary irritation index was given as 1.7, and 2-methoxypropanol-1 was regarded as slightly irritating to the skin (BASF AG 1979 a).

5.3.2 Eyes

Acute eye irritation was investigated using undiluted 2-methoxypropanol-1 in 6 rabbits. A primary irritation index of 16.6 was obtained, and 2-methoxypropanol-1 was regarded as slightly irritating to the eyes (BASF AG 1979 a).

5.4 Allergenic effects

There are no data available.

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

In groups of 5 male Wistar rats, the testis weights were unaffected after gavage doses of 2-methoxypropanol-1 of 1800 mg/kg body weight and day for 10 days (see Section 5.2.2) (BASF AG 1982; Ma-Hock et al. 2005).

5.5.2 Developmental toxicity

The studies of developmental toxicity are described in detail in Table 1.

In a pilot study, groups of 5 rats were exposed to 2-methoxypropanol-1 concentrations of 1000, 2000 or 3000 ml/m^3. A concentration-dependent increase in the number of foetuses with dumbbell-shaped notches of the central cartilage of the thoracic vertebrae was found at concentrations of 1000 ml/m^3 and above (BASF AG 1985, 1986; Hellwig et al. 1994). The rats were found to be less sensitive to the teratogenic effects of 2-methoxypropanol-1 than rabbits (Hellwig et al. 1994). The reason for this is not known.

In rabbits, an increased number of skeletal variations occurred at the low concentration of 143 ml/m^3 and above. Malformation of the sternebrae (bony plate, foetuses: 1/59, 1.7%; litters: 1/10, 10%) occurred in one case at the concentration of 143 ml/m^3. According to the authors, it is questionable whether this was substance-related or a spontaneous occurrence (historical controls: foetuses: 5/2075, 0.24%; litters: 5/340, 1.47%). The findings "bony plate" and "enlarged rib cartilage" reflect a process of advanced ossification and differentiation, the cause of which may be assumed to be substance-related. As a result of the retarded body weight gains at the concentration of 539 ml/m^3, the NOAEC (no observed adverse effect concentration) for maternal toxicity was 356 ml 2-methoxypropanol-1/m^3 (Hellwig et al. 1994). The concentration of 143 ml/m^3 is borderline toxic as regards developmental toxicity and thus very close to the NOAEC for developmental toxicity. The target of teratogenicity at concentrations of 356 ml/m^3 and above is the skeleton; the increased number of skeletal variations occurring even at the low concentration is therefore in accordance.

In a prenatal developmental toxicity study with rabbits carried out according to OECD Test Guideline 414, the main metabolite 2-methoxypropionic acid was teratogenic at a dose level of 78 mg/kg body weight and day. At this dose, the maternal body weight gains were reduced and the number of resorptions increased. The NOAEL (no observed adverse effect level) for developmental toxicity was 26 mg 2-methoxypropionic acid/kg body weight and day, and the NOAEL for maternal toxicity was 78 mg 2-methoxypropionic acid/kg body weight and day (Carney et al. 2003).

In an in vitro study with rabbit whole embryo culture, no significant differences compared with the findings in controls were obtained up to concentrations of 2 mM 2-methoxypropanol-1 and 5 mM 2-methoxypropionic acid, the highest concentrations tested in each case (Carney et al. 2003).

5.6 Genotoxicity

5.6.1 In vitro

In a bacterial mutagenicity test carried out according to OECD Test Guideline 471 using the Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 in the presence and absence of a metabolic activation system (S9 mix from the liver of rats treated with Aroclor 1254), 2-methoxypropanol-1 was not mutagenic either in the standard test or in the pre-incubation test at dose levels between 20 and 5000 µg/plate. The concurrent positive controls yielded the expected results (BASF AG 1992).

Table 1 Studies of the developmental toxicity of 2-methoxypropanol-1 in rats and rabbits

Species, strain, number per group	Exposure	Findings	References
Prenatal developmental toxicity			
rat, Wistar, 5 ♀	**GD 6–15**, 0, 1000, 2000, 3000 ml/m³ (analytical concentrations), 6 hours/day, examination: GD 20, pilot study	**1000 ml/m³**: **NOAEC for maternal toxicity**; **LOAEC for developmental toxicity**; **1000 ml/m³ and above**: foetuses: cartilage notches (thoracic vertebrae); **2000 ml/m³ and above**: dams: mild sedation; **3000 ml/m³**: dams: irritation of the respiratory organs; foetuses: split vertebral bodies (thoracic vertebrae)	BASF AG 1985, 1986

Table 1 (continued)

Species, strain, number per group	Exposure	Findings	References
rabbits, Himalayan, 12 ♀	**GD 6–18**, 0, 143, 222, 356, 539 ml/m³ (analytical concentrations), vapour, whole body, 6 hours/day, examination: GD 29, purity: 98.05%, according to OECD Test Guideline 414	**143 ml/m³: LOAEC for developmental toxicity**; **143 ml/m³ and above**: foetuses: some malformations of the sternebrae (bony plate, foetuses: 1/59; 1.7%; litters: 1/10; 10%), skeletal variations ↑ (trend); **222 ml/m³ and above**: dams: mean uterus weights ↓; foetuses: variations in organs ↑, skeletal anomalies ↑ (trend, not significant; sternum, ribs); **356 ml/m³: NOAEC for maternal toxicity**; dams: dead implants ↑ (not significant), % live foetuses per pregnant animal ↓, % dead implants per pregnant animal ↑; foetuses: mean foetal weight ↓ (not significant), macroscopic variations ↑ (trend; pseudoankylosis, malpositioned or bent toes), skeletal anomalies ↑ (sternum, extremities, ribs); **539 ml/m³**: dams: body weights ↓ as from GD 12, body weight gains ↓ (GD 12–15 and 21–27), abortions in 2/12 (GD 22 and 23), dead implants ↑, % live foetuses per pregnant animal ↓; foetuses: mean foetal weight ↓, placental weights ↑, macroscopic anomalies of the skull (cleft palate, exophthalmus) and of the extremities ↑ (trend), macroscopic variations ↑ (pseudoankylosis, malpositioned or bent toes), anomalies of organs ↑ (trend; truncus arteriosus communis), variations in organs ↑, skeletal anomalies ↑ (sternum, extremities, ribs)	BASF AG 1989; Hellwig et al. 1994

Table 1 (continued)

Species, strain, number per group	Exposure	Findings	References
rabbits, New Zealand White, 20 ♀	**GD 7–19**, 0, 10, 26, 78 mg **2-methoxy propionic acid**/kg body weight and day, gavage, examination: GD 28, purity: 98.6%, according to OECD Test Guideline 414	**10 mg/kg body weight**: **NOAEL for maternal toxicity**; **26 mg/kg body weight**: **NOAEL for developmental toxicity**; dams: body weight gains ↓ (GD 7–10); **78 mg/kg body weight**: dams: body weight gains ↓ (GD 7–20), food consumption ↓; relative kidney weights ↑, resorptions ↑, number of litters with resorptions ↑; foetuses: malformed foetuses ↑ (foetuses: 6/63, litters: 4/11, controls: foetuses: 0/99, litters: 0/16), variations ↑ (retrocaval ureter = abnormal ureter path, retarded ossification of hyoid bone, metatarsal bones, phalangeal (finger) bones of the anterior extremities, irregular ossification of sternebrae)	Carney et al. 2003
In vitro investigations			
rabbits, whole embryo culture	0, 0.5, 2.0 mM **2-methoxy-propanol-1,** purity: 98.9%	**up to 2 mM**: not significantly different from controls	Carney et al. 2003
	0, 1.0, 5.0 mM **2-methoxy-propionic acid**; positive control: 5 mM methoxyacetic acid	**up to 5 mM**: not significantly different from controls; positive controls: somite count ↓, morphology score ↓; number of malformed embryos 100% (controls: 8%)	

GD: gestation day; LOAEC: lowest observed adverse effect concentration; NOAEC: no observed adverse effect concentration; NOAEL: no observed adverse effect level

5.6.2 In vivo

There are no data available.

5.7 Carcinogenicity

There are no data available.

6 Manifesto (MAK value/classification)

The critical effects of 2-methoxypropanol-1 are its irritant effects and teratogenicity.

MAK value. The previous MAK value was set in 2001 in analogy to the previous threshold limit value for 2-ethoxyethanol, which, in the meantime, has been lowered to 2 ml/m^3.

As regards 2-methoxypropanol-1, longer-term inhalation studies are available only for pregnant animals. In a 14-day oral toxicity study in rats, 2-methoxypropanol-1 caused mild anaemia at the dose level of 1800 mg/kg body weight. No NOAEL was obtained; the scope of the study was very limited.

The following toxicokinetic data are taken into consideration for the extrapolation of the estimated NAEL (no adverse effect level) (= LOAEL (lowest observed adverse effect level)/3) of 600 mg/kg body weight and day to a concentration in workplace air: the species-specific correction value for the rat (1:4), the demonstrated oral absorption (100%), the body weight (70 kg) and respiratory volume (10 m^3) of the person, the assumed 100% absorption by inhalation, a possible increase in effects with long-term exposure (1:6) and the extrapolation of the data from an animal study to humans (1:2). The concentration calculated from this is 88 mg/m^3 (23 ml/m^3), and thus, a MAK value of 20 ml/m^3 is obtained using the preferred value approach.

On the basis of the maternal NOAEC of 356 ml/m^3 found in the developmental toxicity study with rabbits, the corresponding concentration would be 15 ml/m^3 taking into consideration the possible increase in the effects during long-term exposure (1:6), the increased respiratory volume at the workplace (1:2) and the extrapolation of the data from an animal study to humans (1:2).

In view of the limited scope of the studies with 2-methoxypropanol-1, the MAK value of 5 ml/m^3 for the better investigated 2-methoxypropylacetate-1, derived on the basis of its irritant effects (see supplement "2-Methoxypropylacetate-1" 2019), is used by analogy for 2-methoxypropanol-1.

The irritant effect of 2-methoxypropanol-1 on the respiratory tract is assumedly less pronounced than that of 2-methoxypropylacetate-1, as irritation has been described at 3000 ml/m^3, but not at the concentrations of 2000 and 1000 ml/m^3 in the developmental toxicity study with rats. On the other hand, with the acetate form, gasping was observed at concentrations of as little as 550 ml/m^3 in the developmental toxicity study with rats. Also with its isomer 1-methoxypropanol-2, the acetate form had a stronger irritant effect on the respiratory tract (supplement "1-Methoxypropylacetat-2" 2000, available in German only). This means that, even when taking into

account the data described above, the MAK value of 5 ml/m³ constitutes a worst case scenario for 2-methoxypropanol-1, so that it has been retained.

Peak limitation. In analogy to 2-methoxypropylacetate-1, Peak Limitation Category I with an excursion factor of 2 has been set for 2-methoxypropanol-1.

Prenatal toxicity. Rabbits were found to be more sensitive to the teratogenic effects of 2-methoxypropanol-1 than rats (Hellwig et al. 1994). In a prenatal developmental toxicity study with rabbits, a dose-dependent increase in skeletal variations without simultaneous maternal toxicity was found even at the lowest concentration of 143 ml/m³, and of skeletal malformations at concentrations of 350 ml/m³ and above (Hellwig et al. 1994). The concentration of 143 ml/m³ is very close to the NOAEC for developmental toxicity. In an oral toxicity study with rabbits using the metabolite 2-methoxypropionic acid, the NOAEL for teratogenicity was 26 mg/kg body weight and day and the NOAEL for maternal toxicity 78 mg/kg body weight and day (Carney et al. 2003).

Taking into account the increased respiratory volume at the workplace in humans compared with that in animals at rest (1:2), the difference between the concentration of 143 ml/m³ in rabbits (which is close to the NOAEC for developmental toxicity) and the MAK value of 5 ml/m³ is 14-fold. The following toxicokinetic data are taken into consideration for the extrapolation of the oral NOAEL of 26 mg 2-methoxypropionic acid/kg body weight and day in rabbits to a concentration in workplace air: the species-specific correction value for the rabbit (1:2.4), the assumed oral absorption of 100%, the body weight (70 kg) and the respiratory volume (10 m³) of the person as well as the assumed 100% absorption by inhalation. The concentration calculated from this is 76 mg/m³ or 20 ml/m³, so that, assuming the complete oxidation of 2-methoxypropanol-1 to 2-methoxypropionic acid, a 4-fold difference to the MAK value of 5 ml/m³ is obtained.

As the differences between the NOAEC and the NOAEL (converted to a concentration in the air) for developmental toxicity and the MAK value are not considered to be sufficient in view of the severity of the effects, 2-methoxypropanol-1 remains assigned to Pregnancy Risk Group B.

Germ cell mutagenicity and carcinogenicity. For the assessment of the genotoxicity of 2-methoxypropanol-1, only one Salmonella mutagenicity test with a negative result is available. There are no studies of the carcinogenicity of 2-methoxypropanol-1. The substance is therefore not classified in one of the categories for germ cell mutagens or carcinogens.

Absorption through the skin. There are no experimental studies available for the penetration of 2-methoxypropanol-1 through the skin. From the theoretical models, it is calculated that 430 to 2600 mg 2-methoxypropanol-1 is absorbed from a 2000 cm² area of skin within one hour. From the available data, a NOAEC for systemic effects of about 15 ml/m³ (56 mg/m³) or 88 mg/m³ can be extrapolated for humans. Assuming complete absorption by inhalation and a respiratory volume of 10 m³ within 8 hours, this NOAEC would correspond to an uptake of 560 or 880 mg 2-methoxypropanol-1 via the airways. Consequently, the estimated dermally absorbed amounts are in the range of the systemically tolerable dose, and therefore at a level at which systemic effects cannot be excluded. Therefore,

2-methoxypropanol-1 remains designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. As there are no data available, the substance is not designated with "Sa" (for substances which cause sensitization of the airways) or "Sh" (for substances which cause sensitization of the skin).

7 References

BASF AG (1979 a) Bericht über die gewerbetoxikologische Grundprüfung von 2-Methoxypropanol-1 (German). BASF Gewerbehygiene und Toxikologie, BASF AG, Ludwigshafen, unpublished report

BASF AG (1979 b) Bericht über die Bestimmung der akuten Inhalationstoxizität LC50 von 2-Methoxypropanol-1 bei 4stündiger Exposition an Sprague-Dawley-Ratten (German). BASF Gewerbehygiene und Toxikologie, BASF AG, Ludwigshafen, unpublished report

BASF AG (1982) Kurzbericht über einen Vorversuch mit 10maliger Sondierung an Ratten mit Ethylglykol, 2-Methoxypropanol-1, 2-Methoxypropanol-1-acetat (German). BASF Gewerbehygiene und Toxikologie, BASF AG, Ludwigshafen, unpublished report

BASF AG (1985) Pränatale Toxizität: Untersuchungen mit 2-Methoxypropylacetat-1, 1-Methoxypropanol-2 und 2-Methoxypropanol-1 (vorläufige Auswertung, Zusammenfassung, Tabellen) (German), 02.05.1985, BASF Gewerbehygiene und Toxikologie, BASF AG, Ludwigshafen, unpublished report

BASF AG (1986) Prenatal toxicity investigation of 2-methoxypropylacetate-1 in rats and rabbits and 2-methoxypropanol-1 in rats. Jan. 1986, BASF Department of Toxicology, BASF AG, Ludwigshafen, unpublished report

BASF AG (1989) Bericht über die pränatale Toxizität von 2-Methoxypropanol-1 an Kaninchen nach inhalativer Aufnahme (German). BASF AG, Abteilung Toxikologie, Project No. 90R0510/8578, BASF AG, Ludwigshafen, unpublished

BASF AG (1992) Report on the study of 2-methoxypropanol-1 in the Ames test. BASF AG, Abteilung Toxikologie, Project No.: 40M0233/914137, BASF AG, Ludwigshafen, unpublished

BUA (Beratergremium für umweltrelevante Altstoffe der Gesellschaft Deutscher Chemiker) (GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance) (1996) Propylenglykolmethylether (German), BUA-Stoffbericht 173, S. Hirzel Verlag, Stuttgart

Buist HE, de Wit-Bos L, Bouwman T, Vaes WHJ (2012) Predicting blood:air partition coefficients using basic physicochemical properties. Regul Toxicol Pharmacol 62: 23–28

Carney EW, Pottenger LH, Johnson KA, Liberacki AB, Tornesi B, Dryzga MD, Hansen SC, Breslin WJ (2003) Significance of 2-methoxypropionic acid formed from β-propylene glycol monomethyl ether: integration of pharmacokinetic and developmental toxicity assessments in rabbits. Toxicol Sci 71: 217–228

ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) (2005) The toxicology of glycol ethers and its relevance to man (fourth edition). Volume I, II, Technical Report No 95, ECETOC, Brussels, Belgium,
http://www.ecetoc.org/publications/technical-reports/

Hellwig J, Klimisch H-J, Jäckh R (1994) Prenatal toxicity of inhalation exposure to 2-methoxypropanol-1 in rabbits. Fundam Appl Toxicol 23: 608–613

Ma-Hock L, Klimisch H-J, Gembardt C, Deckardt K, Jäckh R (2005) Investigations on the subchronic toxicity of 2-methoxypropanol-1(acetate) in rats. Hum Exp Toxicol 24: 95–99

Miller RR, Langvardt PW, Calhoun LL, Yahrmarkt MA (1986) Metabolism and disposition of propylene glycol monomethyl ether (PGME) beta isomer in male rats. Toxicol Appl Pharmacol 83: 170–177

NLM (National Library of Medicine) (2016) 2-Methoxy-1-propanol. Hazardous Substances Data Bank, http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

SRC (Syracuse Research Corporation) (2016) 2-Methoxy-1-propanol, PhysProp database, http://esc.srcinc.com/fatepointer/search.asp

completed March 22, 2017