The MAK-Collection for Occupational Health and Safety

GMS PUBLISSO ZB MED-Publikationsportal Lebenswissenschaften

Methylamine

MAK Value Documentation, supplement – Translation of the German version from 2020

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Keywords

methylamine; nose; irritation; developmental toxicity; maximum workplace concentration; MAK value; momentary value; toxicity; hazardous substance

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated methylamine [74-89-5]. The critical effect is irritation of the nasal airways as observed in a 2-week study in rats with a NOAEC of 75 ml/m^3. The RD_{50} data for methylamine show that its irritation potency is lower than that of other aliphatic amines with a MAK value of 2 ml/m^3. Overall, a MAK value of 5 ml/m^3 has been derived from these data. As the critical effect is local irritation, Peak Limitation Category I has been retained. An excursion factor of 2 has been set by analogy with trimethylamine and cyclohexylamine. For both amines, a momentary value (ceiling limit) was set at two times the MAK value. Therefore, the momentary value of 10 ml/m^3 for methylamine has been retained. The NOAELs for developmental toxicity obtained in an oral screening study in rats (230 mg/kg body weight and day) and a teratogenicity study with i.p. application in mice (155 mg/kg body weight and day) are sufficiently high. Therefore, damage to the embryo or foetus is unlikely when the MAK value is not exceeded and methylamine is classified in Pregnancy Risk Group C. Methylamine is not genotoxic. Carcinogenicity studies are not available. According to calculations, methylamine is not taken up via the skin in amounts that can induce systemic effects. There are no data that show that methylamine is a skin or airway sensitizer.

Citation Note:
Hartwig A, MAK Commission. Methylamine. MAK Value Documentation, supplement – Translation of the German version from 2020. MAK Collect Occup Health Saf. 2022 Jun;7(2):Doc033. https://doi.org/10.34865/mb7489e7_2ad

Manuscript completed:
26 Mar 2019

Publication date:
29 Jun 2022

MAK value (2019)	**5 ml/m³ ≙ 6.4 mg/m³**
Peak limitation (2019)	**Category I, excursion factor 2**
Momentary value (2002)	**10 ml/m³ ≙ 13 mg/m³**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2019)	**Pregnancy Risk Group C**
Germ cell mutagenicity	–
BAT value	–

Synonyms	aminomethane
Chemical name (IUPAC)	methanamine
CAS Number	74-89-5
Structural formula	$CH_3–NH_2$
Molecular formula	CH_5N
Molar mass	31.06 g/mol
Melting point	−93.4 °C (NLM 2018)
Boiling point at 1013 hPa	−6.3 °C (NLM 2018)
Vapour pressure at 20 °C	3140 hPa (ECHA 2018)
log K_{OW}	−0.57 (NLM 2018) −0.713 at 25 °C (ECHA 2018)
Solubility at 25 °C	1080 g/l water (NLM 2018)
pKa value at 25 °C	10.787 (NLM 2018)
1 ml/m³ (ppm) ≙ 1.289 mg/m³	**1 mg/m³ ≙ 0.776 ml/m³ (ppm)**

For methylamine, documentation (Greim 1996) and a supplement (Greim 2002 b, available in German only) are available.

This supplement is based mainly on the publicly available registration data under REACH (ECHA 2018).

Methylamine is a highly water-soluble gas, and is sold in the form of a 40% aqueous solution. To assess the systemic effects of methylamine, also studies with the hydrochloride have been used here.

1 Toxic Effects and Mode of Action

Methylamine is formed endogenously and metabolized to formaldehyde. As an aqueous solution, methylamine is corrosive to the skin and eyes due to its basicity. At concentrations of 250 ml/m³ and above, methylamine was irritating to the respiratory tract of rats after exposure for 2 weeks. The RD_{50} value in mice was found to be 141 ml/m³.

In a study in rats carried out according to OECD Test Guideline 422, the number of corpora lutea and implantations and the litter size were reduced at 1000 mg/kg body weight and day. Methylamine was found to be genotoxic in the mouse

lymphoma test, but only at very high concentrations in the range of the toxicity threshold. Studies of the sensitizing and carcinogenic effects of the substance are not available.

2 Mechanism of Action

The irritant effect is due to the basicity of the substance. The conversion of methylamine to formaldehyde by the semicarbazide-sensitive amine oxidase in the respiratory tract most likely does not play a role in irritation, since the irritant effect of formaldehyde (RD_{50} 3–5 ml/m^3; Greim 2002 a) on the respiratory tract is considerably higher than that of methylamine (RD_{50} 141 ml/m^3; Section 5.1). The same applies to hydrogen peroxide, which is likewise formed during this reaction. This leads to lipid peroxidation, and the malondialdehyde occurring in this process was demonstrated in rats after the administration of methylamine (Deng et al. 1998).

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

Methylamine is formed endogenously. In humans, 11 mg (range 1.68 to 62.3 mg) per day are excreted with the urine (Mitchell and Zhang 2001).

The blood:air partition coefficient, calculated according to the formula of Buist et al. (2012), is 24.7.

The bioavailability of unmetabolized methylamine in F344 rats after oral administration of 18 µmol ^{14}C-labelled methylamine/kg body weight was 69%, the total amount of substance absorbed was 93%. Elimination of methylamine from the blood after intravenous injection of 3 µmol/kg body weight was biphasic and the terminal half-life was 19.1 minutes (Streeter et al. 1990). Methylamine is protonated in the stomach, so that oral absorption of the hydrochloride is likewise assumed to be 93%.

There are no data available for the absorption of the substance through the skin. The data for acute dermal toxicity cannot be used due to the skin damage caused by application of the corrosive substance.

According to ECHA (2018), a 40% aqueous solution of methylamine is corrosive to the skin. For such substances, according to the Classification, Labelling and Packaging Regulation, skin irritation is to be assumed at concentrations of 1% and above. For a non-irritant 0.5% solution, fluxes of 13.7 and 4.4 µg/cm^2 and hour have been calculated with the model of Fiserova-Bergerova et al. (1990) and the algorithm of the IH SkinPerm model using the log K_{OW} of −0.731 (Tibaldi et al. 2014). Assuming the exposure of 2000 cm^2 of skin (hands and forearms) for 1 hour, this corresponds to absorbed amounts of 27.4 and 8.8 mg, respectively.

For exposure to gaseous methylamine at the level of the MAK value, taking into account Henry's constant (H_{pc}) of 0.0000111 atm × m^3/mol (NLM 2018), the concentration in an aqueous film on the skin surface is 0.014 g/l. At this concentration, exposure of the whole body (18 000 cm^2) for 8 hours would result in a dermally absorbed amount of 5.5 mg of methylamine according to the model of Fiserova-Bergerova et al. (1990), or in an absorbed amount of 20.2 mg, calculated with the IH SkinPerm software (AIHA 2019).

The K_m values for the metabolism of methylamine by homogenized umbilical cord aorta and plasma were 832 and 516 µM, respectively, and the V_{max} values were 590 nmol/mg protein and hour and 48 nmol/ml serum and hour, respectively. Metabolism occurred via semicarbazide-sensitive amine oxidase (Lyles et al. 1990).

After ingestion of 2, 4 or 10 g of methylamine hydrochloride, a volunteer excreted about 2% of the dose unchanged with the urine within 24 hours (no other details; US EPA 2008).

3.2 Metabolism

Methylamine can be metabolized by semicarbazide-sensitive amine oxidase in vitro to formaldehyde, hydrogen peroxide and ammonia. Formaldehyde was also detected as a metabolite in rats (Deng et al. 1998; US EPA 2008). The activity of this enzyme is high in the lungs, higher in humans than in rats (US EPA 2008).

In female Wistar rats given intraperitoneal injections of 75 µg ^{14}C-methylamine hydrochloride/kg body weight, 14% of the radioactivity was found in the 24-hour urine, of which 2% as methylurea, and 53% was exhaled in the form of CO_2 within 24 hours. Intestinal microorganisms did not play a role in the metabolism of methylamine (Dar et al. 1985; US EPA 2008).

When administered intravenously to rats, 11% of the methylamine was excreted unchanged with the urine within 72 hours. In addition, formaldehyde, methylurea and formate were detected in the urine (Streeter et al. 1990).

4 Effects in Humans

Secondary sources report odour awareness thresholds of 0.0009 to 9.4 ml/m^3 and irritation thresholds of 7.9 and 18 ml/m^3. More detailed information is not available (US EPA 2008). According to one report, exposure to 10 ml/m^3 was reported to be non-irritating with prolonged exposure, 20 to 100 ml/m^3 was reported to be irritating to the nose, eyes and throat, and higher concentrations were severely irritating (Greim 2002 b; US EPA 2008).

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

The RD_{50} in mice was 141 ml/m^3 (Gagnaire et al. 1989; Greim 2002 b).

The 1-hour LC_{50} for rats was 7110 ml/m^3, the 4-hour LC_{50} for Wistar rats was between 2100 and 2900 mg/m^3 (1630 and 2250 ml/m^3). Irritation of the respiratory tract and eyes was observed (ECHA 2018).

5.1.2 Oral administration

For a 40% solution, the oral LD_{50} in Wistar rats was 698 mg/kg body weight (ECHA 2018).

5.1.3 Dermal application

No data are available.

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

Groups of 10 male Sprague Dawley rats were exposed nose-only to methylamine concentrations of 0, 75, 250 or 750 ml/m^3 (99.9%) for 6 hours daily, on 5 days per week for 2 weeks. Histopathological examinations were performed on 5 animals at the end of exposure and on the remaining 5 animals 2 weeks later. At 75 ml/m^3 and above, red nasal discharge, focal interstitial pneumonitis (but also in the recovery group of controls) and tracheitis (but not in the next-higher concentration group) were found after exposure for 2 weeks. According to the authors, there was mild irritation of the nasal turbinates in the animals of the 75 ml/m^3 group, but the published table does not show that the incidences of the

corresponding histopathological findings were increased compared with those in the controls. At 250 and 750 ml/m^3, the urine pH was decreased, the erythrocyte count increased (not significantly at 250 ml/m^3), and the relative kidney weight was 19% higher. Necrosis or ulceration and regeneration or metaplasia in the respiratory mucosa occurred. These histopathological findings were poorly reversible. At 750 ml/m^3, the animals showed marked clinical signs of irritation, with body weight loss and mortality. Increased relative heart, testis and lung weights, decreased spleen weights and altered blood parameters were also observed. According to the authors, the concentration of 75 ml/m^3 was close to the NOAEC (no observed adverse effect concentration) for systemic and local effects (Kinney et al. 1990 b).

Intra-alveolar and interstitial oedema and interstitial pneumonitis occurred in rats (no other details) exposed continuously to a methylamine concentration of 589 mg/m^3 (490 ml/m^3) for up to 10 weeks (Sriramachari and Jeevaratnam 1994).

5.2.2 Oral administration

Methylamine in the form of a 40% solution was administered daily to male Wistar rats for 21, 45, 65 or 90 days. The doses were 10 mg/kg body weight and day by gavage or 100 mg/kg body weight and day with the diet. There were no effects on body weights or on the weights of the liver, heart, lungs, kidneys and adrenal glands. No gross pathological changes were observed in the organs. The activities of alanine and aspartate aminotransferase, lactate dehydrogenase and alkaline phosphatase were likewise not affected (Sarkar and Sastry 1990). As no histopathological examinations were performed, a NOAEL (no observed adverse effect level) cannot be established from the study.

In a study carried out according to OECD Test Guideline 422 (combined repeated dose toxicity study with reproductive/developmental toxicity screening test), Crl:CD®(SD)IGS BR rats were given daily gavage doses of methylamine hydrochloride (molar mass 67.52 g/mol) of 0, 250, 500 or 1000 mg/kg body weight and day. At 250 mg/kg body weight and day and above, the absolute and relative liver weights of the males were increased (absolute: by 14%, 15%, and 17%, relative: by 11%, 13%, and 21%, respectively), at 500 mg/kg body weight and day and above also in the females (absolute: 18%, 11%, relative: 20%, 15%). At 1000 mg/kg body weight and day, increased relative kidney weights, squamous metaplasia of the tracheal mucosa and focal mucoid metaplasia of the glandular stomach epithelium occurred as signs of local irritation together with decreased body weights. At this dose, parental body weights and food consumption were decreased compared with those in the control animals. The systemic NOAEL was 500 mg methylamine hydrochloride/kg body weight and day (230 mg methylamine/kg body weight), as at 1000 mg/kg body weight and day feed intake and body weights were reduced and the relative kidney weights were increased (OECD 2011).

5.2.3 Dermal application

No data are available.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

Liquefied methylamine was corrosive to the skin of guinea pigs (ECHA 2018).

Studies with aqueous solutions are not available. Due to their basicity, aqueous solutions of methylamine are classified as corrosive, the gas as a skin irritant (ECHA 2018).

5.3.2 Eyes

There are no studies available. Due to its basicity, a corrosive effect of the substance in the eyes is to be assumed.

As a gas or in aqueous solution, the substance is classified as corrosive to the eyes (ECHA 2018).

5.4 Allergenic effects

No data are available.

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

In a study according to OECD Test Guideline 422 (combined repeated dose toxicity study with reproductive/developmental toxicity screening test), methylamine hydrochloride was administered daily by gavage to groups of 12 Crl:CD®(SD)IGS BR rats at doses of 0, 250, 500 or 1000 mg methylamine hydrochloride/kg body weight per day for 98 to 119 days (see also Section 5.2.2). At 1000 mg/kg body weight and day, corpora lutea and implantation numbers and litter size were reduced. Furthermore, decreased body weights and reduced feed intake occurred at this dose. The NOAEL for effects on fertility and parental toxicity was thus 500 mg methylamine hydrochloride/kg body weight and day (230 mg methylamine/kg body weight and day) (OECD 2011). The OECD test guideline specifies dosing on 7 days per week.

Six female Wistar rats were given an oral dose of methylamine of 5 mg/kg body weight and day as an aqueous solution, and mated with untreated males. The average litter size of the treatment group of 6.33 was decreased compared with that of the control group of 8.83. No abnormalities were observed as regards the oestrus cycle, fertility parameters, pregnancy, the number of live births, lactation and the average birth weight (no other data; Sarkar and Sastry 1990). Due to deficiencies in the description of the methods and results, the study is not suitable for assessing the effects of the substance on fertility.

5.5.2 Developmental toxicity

In the documentation from 1984, the methodological shortcomings of a prenatal developmental toxicity study in rats (Greim 1996) were already pointed out.

In another developmental toxicity study, groups of 6 to 8 CD1 mice (29 control animals) were given intraperitoneal injections of methylamine hydrochloride at doses of 0, 0.25, 1.0, 2.5 or 5 mmol/kg body weight and day, corresponding to about 0, 8, 31, 78 or 155 mg methylamine/kg body weight and day, from days 1 to 17 of gestation. The control animals were treated with saline. The dams and foetuses were examined on gestation day 18. No maternal toxicity occurred; the body weights were also not affected. The number of resorptions per litter, the number of live foetuses per litter and the foetal weights were unaffected by the treatment. Skeletal or visceral abnormalities were not found in this study (Guest and Varma 1991). From this study, it may be stated that methylamine hydrochloride in the tested doses does not lead to teratogenic or developmental toxicity. However, due to the unphysiological route of administration, the dose levels used are not suitable for a quantitative assessment of the developmental toxicity when the MAK value is observed.

In embryo cultures, methylamine hydrochloride led to concentration-dependent decreases in yolk sac diameter, crown-rump length, head length, somite number and survival (Guest and Varma 1991).

In the study described in Section 5.5.1 carried out according to OECD Test Guideline 422 in rats (OECD 2011), a complete teratogenicity study was not performed according to the test guideline.

5.6 Genotoxicity

5.6.1 In vitro

Up to the highest non-toxic dose of 2000 µg/plate, methylamine was not mutagenic in the Salmonella typhimurium strains TA98, TA100, TA102, TA104, TA1535, TA1537 and TA1538 and in Escherichia coli WP2uvrA and WP2uvrA/pKM101 with and without the addition of a metabolic activation system (ECHA 2018).

In the $TK^{+/-}$ assay in L5178Y mouse lymphoma cells, a 40% methylamine solution was mutagenic at concentrations of 200 and 300 nl/ml (2.6–3.9 mM) without S9 mix with a maximum 2.5-fold mutant frequency and 40% relative growth compared with the values in the controls. More small colonies were induced than large colonies, suggesting chromosomal damage. The concentration of 400 nl/ml was cytotoxic (Caspary and Myhr 1986). A direct clastogenic effect without metabolic activation seems unlikely due to the structure of the substance. For this test, it is known that pH changes can cause clastogenicity (Cifone et al. 1987). Therefore, the positive result could have been caused by a pH change in the medium due to the alkaline methylamine.

5.6.2 In vivo

In a micronucleus test according to OECD test guideline 474, groups of 5 male NMRI mice were given single gavage doses of methylamine hydrochloride of 0, 500, 1000 or 2000 mg/kg body weight (230, 460, 920 mg methylamine/kg body weight). Evaluation after 24 hours did not yield an increase in the incidence of micronuclei in the polychromatic erythrocytes of the bone marrow. The same result was obtained in another 5 animals that received 2000 mg/kg body weight and which were examined after 48 hours. The ratio of polychromatic to normochromatic erythrocytes was unchanged, 2000 mg/kg body weight resulted in clinical signs of toxicity. The positive controls fulfilled the validity criteria of the test system (ECHA 2018).

In a dominant lethal test, rats were exposed to methylamine concentrations of 0, 0.004, 0.01, 0.053 or 0.270 mg/m³. The duration of exposure was reported to be 1.4 to 428 hours and 5 to 180 days, 4 hours per day (no other data). Concentration-dependent postimplantation losses occurred at concentrations of 0.01 mg/m³ and above. In addition, the semen quality was reduced, the testicular epithelium atrophied and the cycle duration prolonged (ECHA 2018; Greim 1996). The results contradict those of the study according to OECD Test Guideline 422 described in Section 5.5.1. This study, which was published in Russian, is not included in the evaluation of the genotoxicity of methylamine due to shortcomings in the documentation.

5.7 Carcinogenicity

There are no data available for the carcinogenicity of the substance.

6 Manifesto (MAK value/classification)

The critical effect is local irritation.

MAK value. There are no valid studies available for the irritant effects of the substance in humans. The 2-week study in rats (Kinney et al. 1990 b) yielded a LOAEC (lowest observed adverse effect concentration) of 250 ml/m³ and a NOAEC of 75 ml/m³ for findings in the nasal epithelia. From this NOAEC, a workplace concentration of 4 ml/m³ is calculated according to the procedure of Brüning et al. (2014) for the extrapolation of subacute to chronic exposure (1:6) and for the extrapolation of data for local effects from animal experiments to humans (1:3).

Also trimethylamine was investigated by the same authors (Kinney et al. 1990 a). Here, somewhat more pronounced local effects were found at the concentration of 75 ml/m³. The MAK value for trimethylamine was set at 2 ml/m³ in analogy to that for cyclohexylamine, for which there are valid data for sensory irritation in humans. The sensory irritation caused by methylamine is, on the basis of the RD_{50} (141 ml/m³), lower than that of dimethylamine (70 ml/m³, MAK value 2 ml/m³), trimethylamine (61 ml/m³, MAK value 2 ml/m³), and cyclohexylamine (51 ml/m³, MAK value 2 ml/m³). Methylamine has a lower irritation potential than trimethylamine, as shown both in a 2-week study and based on RD_{50} values. These data support the establishment of a higher MAK value for methylamine than for the other amines. Therefore, the MAK value for methylamine is set at 5 ml/m³.

The systemic NOAEC in the 2-week study in rats was 75 ml/m³, as increased relative kidney weights were observed at 250 ml/m³ (= 320 mg/m³, corresponding to a dose of 90 mg/kg body weight at a respiratory volume of 0.8 l/min/

kg body weight and 100% absorption by inhalation). This would result in a MAK value of 2 ml/m^3 (possible increase in effects with chronic exposure (1:6), increased respiratory volume at the workplace (1:2), extrapolation of data from animal experiments to values for humans (1:2)). In the oral study according to OECD Test Guideline 422 in rats, increased kidney weights were likewise observed, which were found, however, at 1000 mg methylamine hydrochloride/kg body weight and day (460 mg methylamine/kg body weight and day). The following toxicokinetic data are taken into consideration for the extrapolation of the systemic NOAEL of 500 mg methylamine hydrochloride/kg body weight and day (230 mg methylamine/kg body weight and day) to a concentration in workplace air: the daily exposure of the animals in comparison with the 5 days per week exposure at the workplace (7:5), the corresponding species-specific correction value for the rat (1:4), the measured oral absorption of 93% (Streeter et al. 1990), the body weight (70 kg) and the respiratory volume (10 m^3) of the person and the assumed 100% absorption by inhalation. The workplace concentration calculated from this is 525 mg methylamine/m^3. When extrapolated from subchronic to chronic exposure (1:2) and from animal experiments to humans (1:2), this corresponds to 131 mg/m^3 (about 100 ml/m^3). The oral test thus produced a considerably higher MAK value for the same end point. It should be noted that the animals were exposed to a higher dose per day for a significantly longer time (about 100 days) than in the 2-week inhalation study. Therefore, the MAK value extrapolated from the 2-week study is to be regarded as the worst case, and 5 ml/m^3 is expected to protect also against systemic effects.

Peak limitation. Assignment to Peak Limitation Category I has been retained, as local irritation is the critical effect. In analogy to trimethylamine and cyclohexylamine, an excursion factor of 2 has been set. Also in analogy to the two better investigated amines, for which a momentary value of about twice the MAK value was set, the previous momentary value of 10 ml/m^3 has been retained for methylamine.

Prenatal toxicity. In the OECD screening test 422 in rats with gavage administration, litter sizes were reduced at a methylamine hydrochloride dose of 1000 mg/kg body weight and day, but not at 500 mg/kg body weight and day. In this test, however, no skeletal and visceral examinations of the offspring were performed as in the case of prenatal developmental toxicity studies (OECD 2011). However, a developmental toxicity study in mice with intraperitoneal injection and detailed examination of the foetuses is available, which indicates that methylamine at high doses is neither developmentally toxic nor does it lead to skeletal or visceral abnormalities (Guest and Varma 1991). Intraperitoneal injection is a worst-case scenario. It can therefore be assumed that likewise no developmental or teratogenic toxicity occurred in the screening test with rats. Both studies together therefore allow a sufficient assessment of the prenatal toxicity of methylamine.

Toxicokinetic extrapolation of the NOAEL of 500 mg methylamine hydrochloride/kg body weight and day (230 mg methylamine/kg body weight and day) results in a concentration at the workplace (see "MAK value" above) of 525 mg methylamine/m^3, which is 82 times as high as the MAK value. The NOAEL of 155 mg methylamine/kg body weight and day from the study with intraperitoneal injection can, however, at best be used as a worst-case scenario for a rough estimate of the embryotoxicity in comparison with the MAK value as a result of the unphysiological route of administration. After toxicokinetic extrapolation (100% intraperitoneal absorption) to a concentration in workplace air, the converted NOAEL would be 155 mg methylamine/m^3, which would correspond to a 24-fold margin to the MAK value. Since the margin between the value obtained in the OECD screening study and the MAK value of 5 ml/m^3 ≙ 6.4 mg/m^3 is sufficiently large and no teratogenicity was found after intraperitoneal administration, methylamine has been assigned to Pregnancy Risk Group C.

Carcinogenicity. There are no carcinogenicity studies available. Methylamine is not genotoxic and, due to its structure, carcinogenic effects are not to be assumed. Methylamine is thus not classified in any of the categories for carcinogens.

Germ cell mutagenicity. Methylamine was not mutagenic in the Salmonella mutagenicity test, and positive results were obtained only at very high concentrations close to the toxicity threshold in the TK$^{+/-}$ test using L5178Y mouse lymphoma cells without metabolic activation. The predominantly small colonies formed in this test are indicative of clastogenicity and could possibly be due to the pH change caused by the alkaline methylamine. In the micronucleus

test, the substance was not clastogenic in the bone marrow of mice. The positive result in vitro was therefore not confirmed in vivo. Studies of mutagenic effects in vivo are not available. Therefore, the substance has not been classified in one of the categories for germ cell mutagens.

Absorption through the skin. For humans, the dermal absorption of a maximum 27.4 mg can be estimated from model calculations (Section 3.1) for exposure to a 0.5% non-irritant solution under standard conditions (2000 cm^2 of skin, exposure for 1 hour). For exposure to gaseous methylamine at the level of the MAK value, the maximum amount absorbed through the skin after 8 hours of whole-body exposure (18 000 cm^2) is 5.5 to 20 mg.

The systemically tolerable concentration of 131 mg/m^3 estimated above corresponds to an absorbed amount of 1310 mg at 100% absorption by inhalation and a respiratory volume of 10 m^3.

Thus, even with simultaneous exposure to methylamine in liquid and gaseous form, dermal absorption makes up less than 25% of the systemically tolerable amount and the substance continues not to be designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. There are no findings available for sensitizing effects in humans and no results from experimental studies in animals or in vitro studies. Methylamine continues not to be designated with either "Sh" or "Sa" (for substances which cause sensitization of the skin or airways).

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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