The MAK Collection for Occupational Health and Safety

Dimethyl sulfoxide (DMSO)

MAK Value Documentation, addendum – Translation of the German version from 2009

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, Geb. 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)*

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Dimethyl sulfoxide / methylsulfinylmethane

MAK Value Documentation

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

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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 work place (MAK value) of dimethyl sulfoxide (DMSO) [67-68-5] of 50 ml/m³, considering the endpoints local and systemic toxicity as well as developmental toxicity. In a 13-week inhalation study the olfactory and respiratory epithelia and the pharynx of rats are the target tissues, and a reduction of body weight gain, possibly secondary to the irritation, is seen. The NOAEC for these effects is 964 mg/m³ (297 ml/m³, vapour). As local effects are critical, the assignment to Peak Limitation Category I and the excursion factor of 2 are confirmed. In a developmental toxicity study with rats a borderline increase in incidences of pups with dilated renal pelvis were seen at the low dose of 200 mg/kg body weight and day. The developmental toxicity study in rabbits revealed an increase in the incidence of malformations of the kidneys after oral administration of 1000 mg/kg body weight and day; this may have been an effect of the treatment. Therefore, a substance-specific effect on the urinary tract cannot be ruled out. Because a NOAEL for developmental toxicity for rats cannot be established, damage to the embryo or foetus cannot be judged and dimethyl sulfoxide is assigned to Pregnancy Risk Group D. DMSO is not genotoxic in vitro and in vivo. Long-term carcinogenicity studies are not available, short-term studies do not indicate a potential for carcinogenicity. DMSO is not a skin sensitizer, data on respiratory sensitization are not available. Skin contact is expected to contribute significantly to the systemic toxicity of DMSO therefore, it is still designated with an "H".

Keywords

dimethyl sulfoxide; methyl sulfoxide; methylsulfinylmethane; DMSO; sulfinylbismethane; mechanism of action; toxicokinetics; metabolism; (sub)acute toxicity; (sub)chronic toxicity; irritation; allergenic effects; reproductive toxicity; developmental toxicity; genotoxicity; carcinogenicity; 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 for Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Geb. 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)

Dimethyl sulfoxide (DMSO)

[67-68-5]

Supplement 2009

MAK value (2008)	**50 ml/m³ (ppm) ≙ 163 mg/m³**
Peak limitation (2008)	**Category I, excursion factor 2**
Absorption through the skin (1990)	**H**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2008)	**Pregnancy Risk Group D**
Germ cell mutagenicity	**–**
BAT value	**–**

Dimethyl sulfoxide was classified in Section IIb of the List of MAK and BAT Values in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992). Since then, new data have become available, making a re-evaluation necessary.

Toxic Effects and Mode of Action

The local effects of dimethyl sulfoxide are the most important. A 13-week inhalation study in rats revealed at 2783 mg/m³ (vapour/aerosol) pseudoglandular changes in the respiratory epithelium, hyperplasia and inflammation of the squamous epithelium, eosinophilic inclusions in the olfactory epithelium of the nose, prominent goblet cells in the pharynx and decreased body weight gains.

Acute and chronic toxicity was low after oral administration and dermal application. Findings in mice, rats, dogs and monkeys included increased diuresis and damage to the liver and kidneys at doses ranging from 1100 to 9900 mg/kg body weight (for 2 to 52 weeks).

Undiluted dimethyl sulfoxide had mildly irritating effects on the skin of guinea pigs after 4-hour occlusive treatment and on the eyes of rabbits after 24 hours.

Dimethyl sulfoxide did not cause sensitization of the skin in humans, mice or guinea pigs or in tests in which dimethyl sulfoxide was used as a solvent control.

Oral studies of developmental toxicity revealed dilation of the renal pelvis in rat foetuses at the maternally non-toxic dose of 200 mg/kg body weight, and above, and renal malformations in rabbit foetuses at the maternally toxic dose of 1000 mg/kg body weight and day.

Dimethyl sulfoxide was not genotoxic in vitro or in vivo.

There are no long-term carcinogenicity studies available for the substance. Initiation–promotion studies provided no evidence of carcinogenic effects.

Toxicokinetics and Metabolism

After rapid dermal absorption, fractions of the dimethyl sulfoxide are reduced to dimethyl sulfide, which is exhaled with a garlic-like odour. Part of the dimethyl sulfoxide fraction not eliminated via the lungs is oxidized to dimethyl sulfone and, with the rest of the dimethyl sulfoxide, is excreted renally. Elimination is biphasic with half-times of 11 to 14 hours for dimethyl sulfoxide and 60 to 70 hours for dimethyl sulfone (documentation "Dimethyl sulfoxide" 1992).

Dimethyl sulfoxide is able to pass the blood–brain barrier (Santos et al. 2003).

Allergenic Effects in Humans

There are no reports available of sensitization caused by dimethyl sulfoxide although it is used in topical formulations.

Animal Experiments and in vitro Studies

Acute toxicity

There are no new data available for acute toxicity.

Subacute, subchronic and chronic toxicity

All the studies published up until 1990 were already described in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992).

The oral doses of between 1100 and 9900 mg/kg body weight administered over periods of 2 to 52 weeks led in mice, rats, dogs and monkeys to tremor, increased diuresis, liver degeneration, lens changes, erosion in the gastrointestinal tract and atrophy of the epithelial and glandular cells in the gastric mucosa. Myopia and lens changes were observed after dermal application in the same dose range (documentation "Dimethyl sulfoxide" 1992).

In a 28-day study carried out according to OECD Test Guideline 412, groups of 5 male and 5 female Crl:CD rats were exposed via their snouts for 6 hours a day, on 7 days a week, to dimethyl sulfoxide concentrations of 0, 125, 500 or 2000 mg/m^3 in vapour form or, in the case of the high concentration group, as a vapour/aerosol mixture. The concentrations determined in the exposure chambers were 0, 132, 507 and 1886 mg/m^3 (corresponding to 0, 41, 156 and 581 ml/m^3). The mass median aerodynamic diameter was 5.1 ± 1.6 µm, and 75% of the aerosol had an aerodynamic diameter of < 7 µm, which the rats were able to inhale. Substance-induced effects on body weights, feed and water consumption or body temperature were not found. There were no gross-pathological changes in the lungs, liver, spleen, kidneys, adrenal glands or testes or any histopathological changes in the nose, larynx, trachea, lungs, liver, stomach or uterus. The NOAEC (no observed adverse effect concentration) was 1886 mg/m^3 (Elf Atochem SA 2000 a).

In a 13-week study carried out according to OECD Test Guideline 413, 10 male and 10 female Crl:CD rats per group inhaled dimethyl sulfoxide concentrations of 0, 310, 964 or 2783 mg/m^3 (corresponding to 0, 95, 297 and 857 ml/m^3) in the form of vapour or, in the case of the high concentration group, a vapour/aerosol mixture produced from 100% dimethyl sulfoxide. The mass median aerodynamic diameter was 5.8 ± 2.2 µm, and 59% of the aerosol had an aerodynamic diameter of < 7 µm, which the rats were able to inhale. In the control and high concentration groups, an additional 10 male and 10 female rats were observed for 4 weeks after the end of treatment to investigate the reversibility of the adverse effects. Another 2 satellite groups were exposed for 6 hours a day, for 28 days. Red discoloration around the nose was a clinical sign observed after treatment in 5 of 10 males and 3 of 10 females of the middle concentration group. This red discoloration around the nose was observed from week 4 onwards in all animals of the high concentration group before and after daily treatment. As there were no concentration-dependent decreases in body weight gains in the female rats, this was not an effect of the test substance. Male body weight gains were decreased in a concentration-dependent manner; this decrease was significant in the high concentration group (Table 1).

Treatment-related ophthalmological changes were not observed. There were no changes in the oestrus cycle, sperm parameters or haematological and urinary parameters. Among the biochemical parameters, the phosphorus level was significantly increased in the male rats of the high concentration group and in the female rats of all groups. The authors did not regard this change as toxicologically relevant because the increases were only slight. The absolute lung weights of the male rats were significantly increased compared with those of the control animals. However, the difference was slight and not concentration-dependent. The histopathological examination revealed treatment-related changes in the nose and pharynx in the high concentration group after 90 days. These consisted of pseudoglandular changes in the respiratory epithelium, inflammation and hyperplasia of the squamous epithelium and an increased number of eosinophilic inclusions in the olfactory epithelium. Goblet cells were observed in the pharyngeal epithelium in 8 of 10 male and 9 of 10 female rats. At the end of the recovery period, these changes were still

Table 1 Changes after 13-week inhalation of dimethyl sulfoxide in rats (Elf Atochem SA 2000 b)

Concentration (mg/m³)	0	310	964	2783
♂				
number of animals examined	10	10	10	10
body weight gain (g)	184	192	166	154[d]
cumulative feed consumption (g)	2656	2681	2516	2403[d]
nose:				
pseudoglandular change in the respiratory epithelium (slight)	0	0	0	7[b]
hyperplasia of the squamous epithelium (minimal)	0	0	0	9[c]
inflammation of the squamous epithelium (minimal)	0	0	0	4
eosinophilic inclusions in the olfactory epithelium:				
minimal	6	9	6	2
slight	0	0	0	4
moderate	0	0	0	4
total	6	9	6	10
pharynx:				
prominent goblet cells	0	0	0	8[c]
♀				
number of animals examined	10	10	10	10
body weight gain (g)	70	58	56	59[d]
cumulative feed consumption (g)	1952	1768[d]	1848[d]	1795[e]
nose:				
pseudoglandular change in the respiratory epithelium (slight)	0	0	0	9[c]
hyperplasia of the squamous epithelium (minimal)	0	0	0	6[a]
inflammation of the squamous epithelium (minimal)	0	0	0	3
eosinophilic inclusions in the olfactory epithelium:				
minimal	5	7	7	0
slight	0	0	0	8
moderate	0	0	0	2
total	5	7	7	10[a]
pharynx:				
prominent goblet cells	0	0	0	9[c]

[a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$ Fisher's exact test
[d] $p < 0.05$; [e] $p < 0.01$ Williams' test (Williams 1971, 1972)

found in the nose as well as in the pharynx of the females of the high concentration group.

In addition, slight myocardial inflammation was observed in the males of the middle and high concentration groups. It is unlikely that this effect was caused by the test substance because it was not detected in females, but was observed with the same level of severity in male control animals at the end of the observation period. The immunotoxicological examinations revealed a dose-dependent increase in antibody-secreting cells in male, but not in female rats; however, the number of such cells varied considerably in the individual animals (Elf Atochem SA 2000 b).

The cause of the red discoloration around the nose is unclear. It might have been caused by the permeability-enhancing effect of dimethyl sulfoxide. The study did not report whether the effect continued to increase after week 5. Weekly behavioural tests revealed brown discoloration of the nose and head, which may correspond to the red discoloration. The frequency of this discoloration was increased only in the males of the high concentration group. However, there was no correlation with the incidence of red discoloration around the nose, which was observed in all animals of this group in week 4 and thereafter; therefore, the observations of brown discoloration are not of use. The authors evidently did not regard the red discoloration around the nose as adverse and did not take it into account for the derivation of the NOAEC.

Because of the histopathological effects on the nose and pharynx and the decrease in body weight gains in the males of the high concentration group, the LOAEC (lowest observed adverse effect concentration) for local and systemic toxicity is 2783 mg/m^3 (aerosol) and the NOAEC for local and systemic toxicity is 964 mg/m^3 (297 ml/m^3) (vapour). However, the above-mentioned red discoloration around the nose was observed at this concentration; the cause of this is unclear. As this effect was not found at 310 mg/m^3 (95 ml/m^3), it has to be assumed that the effect was caused by the test substance, although its adverse nature is not known.

Local effects on skin and mucous membranes

Earlier data were already described in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992).

Undiluted dimethyl sulfoxide was applied occlusively to the skin of 6 guinea pigs for 4, 24, 48 or 72 hours according to OECD Test Guideline 404 and was slightly irritating only after 4 hours (Tenjarla et al. 1995).

Mild irritation was observed after the 24-hour application of 0.1 ml undiluted dimethyl sulfoxide to the rabbit eye (Atofina SA 2003). In another test carried out according to OECD Test Guideline 405, dimethyl sulfoxide induced very mild irritation of the conjunctiva, which was no longer detectable after 3 days (Atofina SA 2003).

Allergenic effects

Earlier data were already described in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992).

Undiluted dimethyl sulfoxide did not cause sensitization in 10 guinea pigs in a maximization test carried out according to OECD Test Guideline 406 (Nakamura et al. 1994). Dimethyl sulfoxide was not sensitizing in either the mouse ear swelling test or the local lymph node assay in mice (Gad et al. 1986; Ikarashi et al. 1993). None of 10 female Hartley guinea pigs was sensitized in a Draize test (induction and challenge treatment with 0.1% dimethyl sulfoxide in physiological saline), a Bühler test, a split adjuvant test, another maximization test or a modified FCA test using cyclophosphamide (induction with 50% dimethyl sulfoxide in ethanol and challenge treatment with 100% dimethyl sulfoxide) (Marzulli and Maguire 1983). Moreover, as extensive negative results are available from studies in which dimethyl sulfoxide was used as a concurrent control solvent, there is no evidence of skin-sensitizing effects in animals.

Reproductive and developmental toxicity

Earlier data were described in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992); however, most of the data do not comply with current requirements.

Developmental toxicity

In a range-finding study of developmental toxicity for the study described below, groups of 7 female SD rats were given gavage doses of dimethyl sulfoxide of 1000, 5000 or 10 000 mg/kg body weight and day from days 6 to 15 of gestation. At 5000 mg/kg body weight and day and above, maternal toxicity was found in the form of reduced feed consumption and decreased body weight gains. Pre-implantation and post-implantation losses and decreases in the number of live foetuses and foetal weights were also observed. The NOAEL (no observed adverse effect level) for maternal toxicity and developmental toxicity is 1000 mg/kg body weight and day (Atofina SA 2003).

In a developmental toxicity study carried out according to OECD Test Guideline 414, groups of 25 pregnant SD rats were given daily gavage doses of dimethyl sulfoxide of 0, 200, 1000 or 5000 mg/kg body weight from days 6 to 15 of gestation and the animals were examined on day 20 of gestation. In the high dose group, the feed consumption and body weight gains of the dams were slightly, but significantly reduced. The foetal weights were also slightly decreased at this dose level. Gross pathological examination revealed the incidences of dilation of the renal pelvis to be increased in all dose groups, but this finding was statistically significant only in the low dose group (8.8%, 5.3% and 5.0% compared with 1.8% in the control group). In addition, the incidence of dilated ureters was increased in animals of the high dose

group. The incidence of skeletal variations or malformations was not increased. As the microscopic examination did not reveal any treatment-related changes in the renal pelvis or ureters of the foetuses, the authors concluded that the gross pathological lesions resulted from a diuretic, but not adverse effect of dimethyl sulfoxide. However, the Commission regards these effects as relevant to the evaluation because the morphology of the foetuses was affected. Reduced ossification of the ribs combined with a decrease in body weights was observed in the foetuses of the high dose group (Elf Atochem SA 1997). In all dose groups, the incidence of dilation of the renal pelvis was only marginally above the standard laboratory range of variation of 0% to 2.8% from 1988 to 1993 or 0.85% to 4.03% from 1995 to 1996. The historical data show that dilation of the renal pelvis has been observed more frequently in more recent times in this rat strain. Nevertheless, the Commission regards this effect as relevant to the evaluation because the kidney is a target organ for malformations also in rabbits. Therefore, 200 mg/kg body weight and day is considered to be the LOAEL (lowest observed adverse effect level) for developmental toxicity and a NOAEL cannot, therefore, be established. The NOAEL for maternal toxicity is 1000 mg/kg body weight and day.

In a study carried out according to OECD Test Guideline 414, groups of 24 pregnant New Zealand White rabbits were given gavage doses of dimethyl sulfoxide of 0, 100, 300 or 1000 mg/kg body weight and day from days 7 to 28 of gestation. The dams and foetuses were examined on day 29 of gestation. During the first 2 days, feed consumption was slightly, but significantly reduced in the middle and high dose groups. Feed consumption and body weight gains were moderately decreased in the high dose group during the first phase of treatment (days 7 to 15 of gestation). The body weight gains were significantly reduced by 37% on the first 2 days of treatment. The proportion of foetuses with non-ossified first ribs (15.8%) was significantly increased in the high dose group. However, this value is only slightly above the maximum of the historical control data (mean: 8.8%; maximum: 14%). The proportion of foetuses with non-ossified fifth ribs was distinctly above the historical control data (mean: 13.3%; maximum: 14.6%) in the low (34%) and high (27.2%) dose groups, but there was no dose–response relationship. However, as the incidence of foetuses with non-ossified fifth ribs per litter was not significantly increased and the incidence of non-ossified first ribs was close to the historical control data, the authors did not regard these changes as adverse, but concluded that embryotoxic or foetotoxic effects were not observed up to the highest dose. The authors established a NOAEL of 1000 mg/kg body weight and day for developmental toxicity and a NOAEL of 100 mg/kg body weight and day for maternal toxicity because feed consumption was reduced at 300 mg/kg body weight and day (Atofina SA 2002 a). At 1000 mg/kg body weight and day, 3 foetuses (1.6%) in 2 litters (10%) were observed with renal malformations, but these were not regarded as treatment-related by the authors. The incidence of renal malformations was somewhat above the standard laboratory range of variation for foetuses (mean: 0.14%; maximum: 0.67%) and for litters (mean: 1.3%; maximum 6.3%). In the control group, 1 foetus had renal malformations, but as this foetus also had other malformations,

the renal malformations in the control foetuses are of only limited relevance for the evaluation. Therefore, in view of the renal findings in the rat foetuses, a possible treatment-related effect cannot completely be ruled out for the high dose in the rabbit study. On the basis of the findings in the renal pelvis, the Commission has established a LOAEL of 1000 mg/kg body weight and day and a NOAEL of 300 mg/kg body weight and day for developmental toxicity in rabbits. The NOAEL for maternal toxicity is 100 mg/kg body weight and day.

Genotoxicity

Dimethyl sulfoxide is used as a solvent in both in vitro and in vivo genotoxicity tests.

The studies listed in the 1990 MAK documentation did not reveal a genotoxic potential of dimethyl sulfoxide. The studies that have been published since then also yielded negative results; they are described below.

In vitro

Dimethyl sulfoxide produced negative results in several SOS chromotests (Mersch-Sundermann et al. 1994) and in an umu test (Atofina SA 2003). In the Salmonella mutagenicity test, dimethyl sulfoxide did not induce mutations in the strains TA98, TA100, TA102, TA104, TA1535, TA1537 or TA1538 in either the presence or absence of metabolic activation (Atofina SA 2003; De Flora 1981; Mersch-Sundermann et al. 1994; Zeiger et al. 1992).

Dimethyl sulfoxide did not lead to SCE (sister chromatid exchange) in CHO cells (a cell line derived from Chinese hamster ovary) up to 5000 µg/ml in either the presence or absence of metabolic activation (Loveday et al. 1990). An UDS test (for unscheduled DNA synthesis) in rat hepatocytes did not demonstrate the induction of DNA repair at dimethyl sulfoxide concentrations of up to 1.4 mol/l (Williams et al. 1989). In a chromosomal aberration test in CHO cells carried out according to OECD Test Guideline 473, chromosomal aberrations were not induced up to 4990 µg/ml in either the presence or absence of metabolic activation (Loveday et al. 1990).

In a micronucleus test in SHE cells (a cell line derived from Syrian hamster embryo) micronuclei were not detected (Fritzenschaf et al. 1993).

In vivo

There was no evidence that dimethyl sulfoxide has genotoxic effects in a test for somatic mutations and recombinations in the eyes of Drosophila melanogaster (Vogel and Nivard 1993). In a micronucleus test in Spanish ribbed newt (Pleurodeles waltl) larvae, micronuclei were not induced after exposure to 138, 275, 550 or 1100 µg/l for 8 or 12 days (Fernandez et al. 1993).

After ICR mice were given single intraperitoneal injections of dimethyl sulfoxide in doses of 0, 2.5, 5.0 or 10.0 ml/kg body weight (0, 2750, 5500 or 11 000 mg/kg body weight) on day 13 of gestation, SCE was not induced in either the foetal liver or the bone marrow of the dams after 24 hours (Atofina SA 2003).

In 8 B6C3F1 mice given single intraperitoneal injections of 5 ml/kg body weight (5500 mg/kg body weight), dimethyl sulfoxide did not cause an increase in micronuclei in the micronucleus test after 24, 48 and 72 hours (McFee et al. 1989).

In a micronucleus test in polychromatic erythrocytes of the bone marrow carried out according to OECD Test Guideline 474, groups of 6 male and 6 female Han-Wistar rats were given 5 intraperitoneal injections at 24-hour intervals with dimethyl sulfoxide doses of 0, 200, 1000 or 5000 mg/kg body weight. The bone marrow was prepared 24 hours after the last treatment. Clinical signs of toxicity were not observed in any dose group. The tests were carried out up to the maximum tolerated dose of 5000 mg/kg body weight that in a range-finding test had caused lethargy and changes in respiration in all animals immediately after administration. In the rats of all dose groups, the PCE/NCE ratio and the number of micronuclei in polychromatic erythrocytes were about the same as those in the rats of the negative control group. The PCE/NCE ratio and the number of micronuclei of the negative control group (water) were in the range of the historical control levels. A statistically significant increase in micronuclei was established in the positive control group (cyclophosphamide; single doses) (Atofina SA 2002 b).

Carcinogenicity

There are no new studies available.

The initiation–promotion studies described in the 1990 documentation (documentation "Dimethyl sulfoxide" 1992) do not provide any evidence of carcinogenicity.

Manifesto (MAK value/classification)

Study data for exposed persons are not available for the derivation of a MAK value. A 13-week inhalation study in rats with dimethyl sulfoxide revealed pseudoglandular changes in the respiratory epithelium, hyperplasia and inflammation of the squamous epithelium and eosinophilic inclusions in the olfactory epithelium of the nose in male and female animals at 2783 mg/m^3 (vapour/aerosol mixture). Male body weight gains were slightly reduced, which may have been a non-specific response to irritation because there were no other signs of systemic toxicity. The NOAEC for the histopathologically detected effects on the nasal epithelium was 964 mg/m^3 (297 ml/m^3). The NOAEC was lower after prolonged exposure (NOAEC: 1886 mg/m^3 after 28 days compared with 964 mg/m^3 after 13 weeks). Therefore, the MAK value has been established at 50 ml/m^3. Although clinical signs

(red discoloration around the nose) were observed in about half of the animals at 964 mg/m³ (297 ml/m³), it is unclear whether this was an adverse effect. Red discoloration around the nose was not observed at 310 mg/m³ (95 ml/m³). The MAK value thus also provides protection against this effect.

Dimethyl sulfoxide is classified in Peak Limitation Category I because the local effects on the nose are of the most importance. As the difference between the MAK value and the NOAEC for histopathological findings is sufficiently large, an excursion factor of 2 has been established.

In a valid study of developmental toxicity in rats, the incidence of dilation of the renal pelvis was increased in all dose groups. The LOAEL for developmental toxicity in rats is therefore 200 mg/kg body weight and day. Assuming 100% absorption, a body weight of 70 kg and a respiratory volume of 10 m³, this corresponds to 431 ml/m³ for exposed persons. As the increased incidences of dilation of the renal pelvis were close to the historical control values and were not clearly dose-dependent, the relevance of these findings is unclear. The developmental toxicity study in rabbits revealed an increase in the incidence of malformations of the kidneys after oral administration of 1000 mg/kg body weight and day; this may have been an effect of the treatment. Therefore, a substance-specific effect on the urinary tract cannot be ruled out. Dimethyl sulfoxide has been classified in Pregnancy Risk Group D because it was not possible to establish a NOAEL for developmental toxicity based on the effects in rats. Another study in rats might clarify the findings obtained in the renal pelvis.

Studies of carcinogenicity are not available, and initiation–promotion studies provided no evidence of carcinogenic effects. Dimethyl sulfoxide did not induce genotoxic effects. Therefore, dimethyl sulfoxide has not been classified in one of the carcinogen categories or in any of the germ cell mutagen categories.

Dimethyl sulfoxide is still designated with an "H" (for substances which can be absorbed through the skin).

In the case of co-exposure, an absorption-enhancing effect may generally be assumed.

There are no reports of contact sensitization in humans although there may be exposure to dimethyl sulfoxide in topical formulations. In view of the negative results in experiments with dimethyl sulfoxide in guinea pigs and the large number of studies in which dimethyl sulfoxide was used as a solvent and control, the substance is likewise not suspected of causing sensitization of the skin in animals. There are no data available for sensitization of the respiratory tract. Therefore, dimethyl sulfoxide has not been designated with either "Sa" or "Sh" (for substances which cause sensitization of the airways and skin).

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