

The MAK Collection for Occupational Health and Safety

Magnesium oxide, insoluble (Sintermagnesite) (respirable fraction)

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

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Keywords: magnesium oxide; MAK value; maximum workplace concentration; general limit value for dust, respirable fraction; peak limitation; developmental toxicity; carcinogenicity

Citation Note: Hartwig A, MAK Commission. Magnesium oxide, insoluble (Sintermagnesite) (respirable fraction). 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):374-381]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2025. https://doi.org/10.34865/mb130948stae6519_w

Republished (online): 08 Aug 2025

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; <https://doi.org/10.1002/3527600418.mb130948stae6519>

Addendum completed: 22 Mar 2017

Published (online): 25 Apr 2019

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



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Magnesium oxide, insoluble (Sintermagnesite)¹⁾ (respirable fraction)

MAK Value Documentation

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DOI: 10.1002/3527600418.mb130948stae6519

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has reevaluated magnesium oxide. Magnesium oxide, sintermagnesite [1309-48-4], is a biopersistent granular dust. Therefore, the respirable fraction of magnesium oxide dust has been classified in Carcinogen Category 4 and a MAK value of $0.3 \text{ mg/m}^3 \times \text{material density}$ was established for the respirable fraction in analogy to the other biopersistent granular dusts. Additionally for this fraction the Peak Limitation Category II with an excursion factor of 8 was established. Since magnesium oxide is not systemically distributed and accumulates only locally in the lungs, no developmental effects due to this dust are expected to occur at the MAK value of $0.3 \text{ mg/m}^3 \times \text{material density}$ (respirable, R-fraction). Magnesium oxide has accordingly been classified in Pregnancy Risk Group C. Magnesium oxide is not designated with either “Sa” or “Sh” or “H”.

Keywords

magnesium oxide; magensia; sintermagnesite; mechanism of action; toxicokinetics; metabolism; (sub)acute toxicity; (sub)chronic 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

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¹⁾ The reevaluation refers exclusively to highly glowing MgO (dead burned respectively sintermagnesite), except for ultrafine particles; see section V h of the List of MAK and BAT Values.

Magnesium oxide, insoluble (Sintermagnesite)¹⁾ (respirable fraction)

[1309-48-4]

Supplement 2018

MAK value (2017)	0.3 mg/m³ R × material density²⁾
Peak limitation (2017)	Category II, excursion factor 8
Absorption through the skin	–
Sensitization	–
Carcinogenicity (2017)	Category 4
Prenatal toxicity (2017)	Pregnancy Risk Group C
Germ cell mutagenicity	–

Chemical name	magnesium oxide
Molar mass	40.32 g/mol
Density	3.58 g/cm ³ (25 °C) (IFA 2015)
Solubility	dead burned MgO is practically insoluble in water (IFA 2015)

Since the first documentation published in 1985 (documentation “Magnesium oxide” 1991) and the 1999 and 2009 supplements (supplement “Magnesium oxide” 1999; supplement “Magnesium oxide” 2009), the threshold limit value for the R fraction of biopersistent granular dusts (supplement “General threshold limit value for dust (R fraction) (Biopersistent granular dusts)” 2012) has been lowered. In the following, it is assessed whether magnesium oxide belongs to the class of biopersistent granular dusts.

1) The supplement refers exclusively to dead burned MgO/sintermagnesite, except for ultrafine particles; see section V h of the List of MAK and BAT Values.

2) The effect of magnesium oxide is based on the effect of biopersistent granular dusts. The value of 0.3 mg/m³ for the R fraction applies to a material density of 1 g/cm³.

General remarks

Magnesium oxide (MgO) is formed in addition to magnesium nitride (Mg₃N₂) when magnesium is burned. Pure magnesium oxide is obtained when magnesium hydroxide or magnesium carbonate is burned. When the reaction takes place at temperatures of up to 900 °C, a compound which reacts with water, so-called “caustic magnesia” (“light burned”) is formed. A chemically inert magnesium oxide (“dead burned”) which is stable at high temperatures and is used in the production of fire-proof stones and crucibles is formed only when heated to above 1600 °C by means of sintering processes. It is estimated that approximately 65% of the total MgO used is required for high-temperature processes, mainly in the iron and steel industries. Magnesium oxide crystallizes in the cubic NaCl structure.

1 Toxic Effects and Mode of Action

Magnesium oxide particles can be taken up by inhalation and ingestion. Absorption through the skin is not known. Sintered MgO particles are chemically inert. They are poorly soluble dusts which, like biopersistent granular dusts, cause the general effects known for particles. Like other inhaled poorly soluble dusts, these particles are able to accumulate in the lungs and the lymph nodes, and cause impairment of the clearance function of the lungs (supplement “General threshold limit value for dust (R fraction) (Biopersistent granular dusts)” 2012).

No genotoxic effects are known for magnesium oxide.

As magnesium oxide particles are poorly soluble biopersistent granular dusts, particle-induced tumour formation is to be expected when lung clearance is overloaded.

Magnesium oxide has no toxic effects on reproduction and is not sensitizing (see supplement “Magnesium oxide” 2009).

In the studies cited below, the precise form of the magnesium oxide used is not clearly specified. These studies are therefore of only limited relevance to the assessment.

2 Mechanism of Action

See supplement “General threshold limit value for dust (R fraction) (Biopersistent granular dusts)” 2012.

3 Toxicokinetics and Metabolism

See supplement “General threshold limit value for dust (R fraction) (Biopersistent granular dusts)” 2012.

4 Effects in Humans

4.1 Single exposures

In a study, 6 volunteers were exposed to magnesium oxide fume and monitored via a face mask with an open mouthpiece. Three of the volunteers were former smokers. The particles in the fume were of different sizes: 28% had a diameter of $< 0.1 \mu\text{m}$, over 98% had a diameter of below $2.5 \mu\text{m}$. To obtain different cumulative magnesium doses for the individual volunteers (from a minimum 261 to a maximum $6435 \text{ min} \times \text{mg}/\text{m}^3$), different exposure durations (15 to 45 minutes) and concentrations (5.8 to $230 \text{ mg}/\text{m}^3$, median concentration $133.0 \text{ mg}/\text{m}^3$) were selected for the 6 volunteers. Lung function, peripheral blood and the bronchoalveolar lavage (BAL) of the participants were examined 18 to 20 hours after the exposure. Each participant was his own control. The control (base) values for lung function and peripheral blood were recorded prior to the start of the exposure and the BAL 28 days after the end of the exposure. There was no change in lung function, including the CO diffusion capacity, in any of the volunteers. No changes were found in the blood count or in the number of polymorphous nuclear leukocytes (granulocytes). In the BAL, no significant differences compared with the control data were found for the interleukin concentrations (IL-1, IL-6, IL-8), the tumour necrosis factor, the number of neutrophils, macrophages and lymphocytes, or the protein content. The authors concluded that even in the BAL the short-term exposure of a maximum 45 minutes to a mixture of fine and ultrafine MgO at high concentrations did not produce any measurable inflammatory reactions in the lungs (Kuschner et al. 1997).

4.2 Repeated exposure

In a review, a small number of epidemiological studies with workers in the magnesite-processing industry were described. The workers were exposed either to magnesite dust (MgCO_3) in mines or to the dust aerosol during calcination of the magnesite ore at about 800°C . Magnesite ore contains mainly MgO. Analysed dust samples contained up to 88.52% magnesium oxide, but also iron oxide, calcium oxide, aluminium oxide and quartz. In these studies, there was an increase in cases of chronic bronchitis and significantly increased incidences of gastric and intestinal ulcers; the increases were dependent on the duration of dust exposure. In another study, the magnesium concentrations in the serum of the volunteers were 3 times higher than normal. In addition, there were increased incidences of pulmonary emphysema and chronic bronchitis. In this study, the participants were monitored for a period of one year. The original studies referred to in the review are not available (review: Reichrtová and Takác 1992). The data cannot be used for the evaluation as the persons involved were exposed to a mixture of substances.

4.3 Local effects on skin and mucous membranes

There are no new data available.

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4.4 Allergenic effects

There are no new data available.

4.5 Reproductive and developmental toxicity

There are no new data available.

4.6 Genotoxicity

There are no new data available.

4.7 Carcinogenicity

In a Norwegian plant producing magnesium metal, a study of the incidence of cancer was carried out in a cohort of 2391 male workers. Only those workers were included in the study who had worked in the plant for at least one year between 1951 and 1974. In total, the study comprised 52 733 person years. The cohorts were observed from 1953 to 1984. In this period, altogether 152 new cancer cases occurred, compared with 132.6 expected cases. In the lungs, 32 cases of cancer were found, compared with 18.2 expected cases. Of the 2391 workers, 393 were exposed mainly to magnesium oxide and coal dust (categorized according to the duration of exposure). In this exposure group there were 35 new cases of cancer, compared with 25.2 expected cases. From this, an increased SIR of 1.4 (95% confidence interval 1.0–1.9) was calculated, which is of borderline statistical significance. The increase in the incidences of lung and stomach cancer was approximately double the expected number of cases; the increase was, however, not statistically significant. The manufacturing process is described in this study. Temperatures of 1100 to 1200 °C were reached during this process. This means that in this study sintered (dead burned) MgO was not involved. In addition, the workers were exposed to a mixture of substances including asbestos, polycyclic aromatic hydrocarbons, coal tar and hexachlorobenzene (Heldaas et al. 1989).

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

There are no new data available.

5.2 Subacute, subchronic and chronic toxicity

Groups of 48 hamsters received 3 mg MgO (not further specified) of varying particle size by intratracheal instillation once a week for life. The particle sizes were mostly between 1 and 25 µm: 90% of the particles were < 25 µm, 46% < 10 µm, 18% < 5 µm and 1% < 1 µm in size. At the end of treatment the histopathological examinations

revealed slight metaplasia in the tracheobronchial zone and moderate hyperplasia of the alveolar zone (no other details, NTP 2001).

5.3 Local effects on skin and mucous membranes

There are no new data available.

5.4 Allergenic effects

There are no new data available.

5.5 Reproductive and developmental toxicity

There are no new data available.

5.6 Genotoxicity

Magnesium oxide particles with a mean size of 3.6 μm were tested in a bacterial mutagenicity assay with the *Salmonella typhimurium* strain TA102. Concentrations of 0, 2.5, 5 or 10 mg/ml were used. MgO was not mutagenic either with or without metabolic activation (Sawai et al. 1998).

5.7 Carcinogenicity

The results of a carcinogenicity study in rats with subcutaneous administration of MgO (not further specified) were described as negative. However, no details were given regarding the dose and scope of the study (Maltoni et al. 1991).

5.8 Other effects

In endothelial cells from human umbilical veins, MgO concentrations above 500 $\mu\text{g/ml}$ (particles mainly 100 nm in size) for periods of 1, 3, 5 and 7 days induced time-dependent cytotoxic effects in the MTT test (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide test). In addition, an increase in the NO concentration in the cells was found at MgO concentrations of 200 $\mu\text{g/ml}$ and above after 24 hours. Theoretically, the increased NO concentration is able to improve thrombocyte/leukocyte adhesion, thus reducing damage to the cells. The study showed that MgO nanoparticles in vitro are cytotoxic only after high concentrations (Ge et al. 2011).

In RAW-264.7 cells, a macrophage-like murine cell line, MgO nanoparticles (no other details) with a mean particle size of 8 nm in concentrations of 1, 5, 10, 40 and 80 $\mu\text{g/cm}^2$ did not produce apoptosis over periods of 4, 6 and 24 hours (Wilhelmi et al. 2012).

6 Manifesto (MAK value/classification)

MAK value. Sintered magnesium oxide (“dead burned”, sintermagnesite) is practically insoluble and affects the lungs after inhalation due to the general particle effects of biopersistent granular dusts. Magnesium is an essential trace element. In humans, magnesium compounds are taken up orally on a widespread basis in the form of food additives and pharmaceuticals, also in the form of self-medication. As sintered magnesium oxide is practically insoluble and therefore practically not bioavailable, no effects on magnesium homeostasis and no systemic effects are to be expected from inhaling the dust. Therefore, the general threshold limit value for dust of $0.3 \text{ mg/m}^3 \times \text{material density}$ for the respirable fraction applies in the case of magnesium oxide dust. If the results of the controlled clinical study of Kuschner et al. (1997) (133 mg/m^3 for 45 minutes without effects) are extrapolated in linear fashion to the resultant threshold value of 1 mg/m^3 (0.3×3.58), no effects should be detectable in the BAL even after exposure at the level of this threshold value for more than 10 days (8 hours/day). This estimate supports the application of the threshold limit value for biopersistent granular dusts in the case of sintered magnesium oxide. For the inhalable fraction, the previous value of 4 mg/m^3 has been retained, as there are no new data available for a re-evaluation.

Peak limitation. The critical effect is the effect of biopersistent granular particles on the lungs. Magnesium oxide dust, like other granular dusts, is assigned to Peak Limitation Category II. As the clearance half-life of biopersistent granular dusts is about 400 days, an excursion factor of 8 has been set.

Prenatal toxicity. There are no studies available for the developmental toxicity of magnesium oxide. As magnesium oxide is a poorly soluble dust, no prenatal toxicity is to be expected when the MAK value of $0.3 \text{ mg/m}^3 \times \text{material density}$ is observed. Therefore, in analogy to other biopersistent granular dusts, the substance is classified in Pregnancy Risk Group C.

Carcinogenicity. There are no epidemiological studies available. As magnesium oxide is a practically insoluble biopersistent granular dust, particle-induced tumour formation after inhalation cannot be excluded in rats. Inflammation in the alveolar or bronchial region, which is accompanied by the release of reactive oxygen species, is mainly responsible for this. Studies like those with biopersistent granular dusts are, however, not available. In analogy to other biopersistent granular dusts, the respirable fraction of magnesium oxide dust is classified in Carcinogen Category 4.

Germ cell mutagenicity. The available data for genotoxicity do not indicate that magnesium oxide dust causes germ cell mutagenicity. Therefore, in analogy to other biopersistent granular dusts, the substance is not classified in one of the categories for germ cell mutagenicity.

Absorption through the skin. The absorption of magnesium oxide through the skin is not known. In analogy to other biopersistent granular dusts, the substance is not designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. There is no evidence that magnesium oxide causes sensitization of the skin or airways. In analogy to other biopersistent granular dusts, magnesium oxide is therefore not designated with either “Sh” or “Sa” (for substances which cause sensitization of the skin or airways).

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completed March 22, 2017