

Graphite (respirable fraction)

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

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)

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Abstract

The German Commission for the Investigation of Health Hazards of Chemicals in the Work Area has re-evaluated graphite [7782-42-5]. Graphite is a granular biopersistent dust. Therefore, the respirable fraction of graphite is classified in Carcinogen Category 4 and a maximum concentration at the workplace (MAK value) of $0.3 \text{ mg/m}^3 \times \text{material density}$ is established by analogy with other granular biopersistent dusts. Additionally, this fraction is classified in Peak Limitation Category II with an excursion factor of 8. Since graphite is not systemically distributed and accumulates only locally in the lungs, damage to the embryo or foetus is unlikely when the MAK value is not exceeded. Accordingly, the classification in Pregnancy Risk Group C is confirmed. Graphite is not a sensitizer and is not taken up via the skin in toxicologically relevant amounts.

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MAK value (2019)	0.3 mg/m³ × material density R^{a)}
Peak limitation (2019)	Category II, excursion factor 8
Absorption through the skin	–
Sensitization	–
Carcinogenicity (2019)	Category 4
Prenatal toxicity (1994)	Pregnancy Risk Group C
Germ cell mutagenicity	–
BAT value	–
CAS number	7782-42-5
EINECS number	231-955-3
Formula	C
Molar mass	12.007 g/mol
Density	2.2 g/cm ³ (IFA 2018)
Solubility	insoluble in water and acids (Greim 2002)

^{a)} The effect of graphite 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

Note: ultrafine particles are excluded; see List of MAK and BAT Values, Section V h (DFG 2019).

Since the last documentation (Greim 2002, available in German only), the general threshold limit value for the respirable fraction of biopersistent granular dusts (Hartwig 2014) was lowered in 2011. This supplement examines whether graphite belongs to the group of biopersistent granular dusts.

Toxic Effects and Mode of Action

See the last documentation (Greim 2002).

Graphite particles are poorly soluble dusts which, in the same way as biopersistent granular dusts, cause general particle effects in the lungs. Like other inhaled poorly soluble dusts, the particles can accumulate in the lungs and lymph nodes and impair the clearance function in the lungs (Hartwig 2014).

Genotoxic effects of graphite are unknown.

There are no long-term studies of the carcinogenic effects of graphite. Since graphite particles are biopersistent granular dusts, particle-induced tumour formation is to be expected when lung clearance is overloaded.

There are no data available for the reproductive toxicity and sensitizing effects of graphite.

Mechanism of Action

Since graphite represents a biopersistent granular dust, particle-induced tumour formation in the lungs of rats is to be expected after inhalation exposure. This is due mainly to inflammation in the alveolar or bronchial region, which is accompanied by the release of reactive oxygen species (Hartwig 2014).

Animal Experiments and in vitro Studies

Acute toxicity

Lung function and inflammation in the lungs were studied in rats after exposure to smoke produced by the combustion of carbon-graphite composite. Male Fischer 344 rats (146 animals) were exposed to the smoke at a concentration of 26.8–29.8 g/m³ by inhalation for 1 hour and examined 1, 2, 3 and 7 days after the end of exposure. Histopathological examination did not reveal any acute damage to the lungs. A statistically significant increase in TNF- α (tumour necrosis factor- α) and MIP-2 (macrophage inflammatory protein) in the bronchoalveolar lavage fluid (BALF) was found after 1 day. In the lung tissue, the expression of TNF- α and MIP-2 was increased as well as that of interferon- γ . In addition, a pronounced increase in neutrophil invasion in the BALF was observed (Whitehead et al. 2003).

In another study, 49 guinea pigs were exposed to the same smoke. Over a period of 30 minutes they were exposed to combustion products of 2, 5, 10 and 100 g of the material. After treatment, the animals were characterized only by their respiratory behaviour. Changes in respiratory behaviour characteristic of acute asthmatic reactions and bronchoconstriction were observed. In the high concentration group, also convulsion occurred. All symptoms normalized after breathing clean air. The respiratory behaviour in the animals of the low concentration group was normal (Kimmel et al. 2002).

Since the animals in the two studies were not exposed to graphite but to its combustion products, the results cannot be included in the evaluation of the source material.

Manifesto (MAK value/classification)

The critical effect of graphite dust is the non-specific particle effect on the lungs.

MAK value. Graphite dust is poorly soluble and acts on the lungs after inhalation exposure due to the general particle effect of biopersistent granular dusts on the lungs. For micro-scale graphite dust particles, there are no findings of substance-specific toxicity (see Greim 2002). For graphite dust, the general threshold limit value for dust of 0.3 mg/m³ \times material density for the respirable fraction applies.

Peak limitation. The critical effect is the effect of biopersistent granular dusts on the lungs. For this reason, the respirable fraction of graphite dust, like that of other biopersistent granular dusts, has been assigned to Peak Limitation Category II. Since 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 developmental toxicity studies available for graphite. Since graphite is a poorly soluble dust, prenatal toxicity is not to be expected if the MAK value is observed. Therefore, by analogy with other biopersistent granular dusts, assignment to Pregnancy Risk Group C has been retained.

Carcinogenicity. Since graphite is a biopersistent granular dust, particle-induced tumour formation after inhalation is to be expected in rats. This is due mainly to inflammation in the alveolar or bronchial regions, which is accompanied by the release of reactive oxygen species. The respirable fraction of graphite is therefore assigned to Carcinogen Category 4 like that of other biopersistent granular dusts.

Germ cell mutagenicity. There are no data available for the genotoxicity of graphite. Therefore, by analogy with other biopersistent granular dusts, the substance has not been classified in one of the categories for germ cell mutagens.

Absorption through the skin. Dermal absorption of graphite is unknown. Like other biopersistent granular dusts, the substance has not been designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. There are no clinical findings of sensitizing effects of graphite on intact skin in humans and no positive results from experimental studies in animals. Likewise, there is no evidence of a sensitizing effect of graphite on the airways. By analogy with other biopersistent granular dusts, graphite has therefore not been designated with “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 (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

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