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Oleoyl sarcosine

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

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Keywords

oleoyl sarcosine; lung fibrosis; inflammation; epiglottis; toxicity; MAK value; maximum workplace concentration; peak limitation; irritation

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) of oleoyl sarcosine [110-25-8]. Critical effects are lung fibrosis and inflammation at the epiglottis in rats in a 28-day study at an aerosol concentration of 6 mg/m^3, the lowest concentration tested. A $BMDL_{05}$ of 1.3 mg/m^3 as surrogate for a NOAEC for fibrosis had been calculated. For inflammation at the epiglottis an NAEC of 2 mg/m^3 was estimated. Taken together, a MAK value of 0.1 mg/m^3 had been set. Since the NAEC for inflammation at the epiglottis is similar to the $BMDL_{05}$ for lung toxicity, the MAK value had been established for the inhalable fraction (I). The MAK value is now lowered to 0.05 mg/m^3 (I) considering the increased respiratory volume at the workplace (see List of MAK and BAT Values, Sections I b and I c). Oleoyl sarcosine remains assigned to Peak Limitation Category II because the fibrosis is considered not to result from an immediate irritation. As the half-life in the lung is not known, the default excursion factor of 2 is retained. There are still no data on sensitization of the airways, no clinical evidence and only an equivocal result from a maximization test for skin sensitization.

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MAK value (2017)	**0.05 mg/m³ I (inhalable fraction)**
Peak limitation (2014)	**Category II, excursion factor 2**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2014)	**Pregnancy Risk Group D**
Germ cell mutagenicity	–
CAS number	110-25-8
Vapour pressure at 20 °C	0.0000004 hPa (Greim 2001)

This supplement has been drawn up to examine the applicability of calculating a Human Equivalent Concentration (HEC); this was used to support the derivation of the MAK value for the substance in 2014 (Hartwig 2015, available in German only).

Conclusions cannot be drawn by analogy to other fatty acid acyl sarcosines, as no inhalation studies are available for them (CIR 2016).

Effects in Humans

Allergenic effects

There are no findings available.

Animal Experiments and in vitro Studies

Subacute, subchronic and chronic toxicity

Inhalation

In a 28-day inhalation study, oleoyl sarcosine caused an early stage of fibrosis in the lungs and submucosal inflammation of the epiglottis in rats even at the lowest aerosol concentration tested of 6 mg/m³. A benchmark calculation for the end point "early stage of fibrosis of the alveolar walls" for male and female rats yielded a $BMDL_{05}$ (benchmark dose lower confidence limit) of 1.3 mg/m³. In view of the effects on the epiglottis in one male and one female animal of the 6 mg/m³ group, the NOAEC (no observed adverse effect concentration) for effects outside the lungs is probably 2 to 3 mg/m³ (Hartwig 2015).

Allergenic effects

A skin sensitizing potential of oleoyl sarcosine cannot be deduced with sufficient certainty from an equivocal result in a maximization test (Greim 2001).

More recent data are not available.

Manifesto (MAK value/classification)

The critical effects of oleoyl sarcosine are lung fibrosis, inflammation of the epiglottis in rats and irritation of the eyes and skin (Greim 2001).

MAK value. In a 28-day study, oleoyl sarcosine caused an early stage of fibrosis in the lungs and submucosal inflammation of the epiglottis of rats at the lowest aerosol concentration tested of 6 mg/m^3 and above. The authors suspected that the early stage of fibrosis observed in the lungs would increase with exposure for a longer period.

Respirable (R) fraction

As undiluted oleoyl sarcosine caused skin and eye irritation (Greim 2001), it should not be considered an inert substance. Although the substance is poorly soluble in water (0.44 mg/l; Hartwig 2015), it is not completely insoluble. The 28-day study was conducted with an aerosol of oleoyl sarcosine dissolved in aqueous ethanol. Although it is possible to calculate the different deposition fractions in the alveoli of rats and humans using the MPPD (multiple-path particle dosimetry) model and to derive a HEC, a HEC has not been calculated because the substance is not an inert dust and it is not known how the solubility of oleoyl sarcosine in the lungs affects the elimination half-lives in rats and humans.

A benchmark calculation for the end point "early stage of fibrosis of the alveolar walls" for male and female rats yielded a $BMDL_{05}$ of 1.3 mg/m^3 (Hartwig 2015). As this value is derived from studies in experimental animals, a MAK value of 0.05 mg/m^3 R can be calculated in accordance with the procedure of the Commission (see List of MAK and BAT Values, Section I), taking into consideration a possible increase in the effects with long-term exposure (1:6), the increased respiratory volume at the workplace (1:2) and the extrapolation of the data from the animal experiment to humans (1:2). This value is higher than the vapour saturation concentration of 0.006 mg/m^3, so that the substance is present as an aerosol at the concentration of the MAK value.

Inhalable (I) fraction

The NAEC (no adverse effect concentration) for effects outside the lungs is expected to be about 2 mg/m^3. This estimate is based on the assumption that the NAEC is around one third of the LOAEC (lowest observed adverse effect concentration) (ECETOC 2010). As this value is derived from animal studies, a value of about 0.2 mg/m^3 for the inhalable fraction can be derived in accordance with the procedure of the Commission (see List of MAK and BAT Values, Section I) and taking into consideration a possible increase in the effects over time (Hartwig 2015). Since the NOAEC has only been estimated and a higher level of extrathoracic deposition is to be expected for the I fraction due to the higher MMAD (mass median aerodynamic diameter), the MAK value for the I fraction has likewise been set at 0.05 mg/m^3 I.

Since the I fraction includes also the R fraction, the MAK value is established only for the I fraction.

Peak limitation. Since the critical effect occurs at the entrance to the respiratory tract, but not directly in the form of an irritant effect, oleoyl sarcosine remains assigned to Peak Limitation Category II. As data for the half-life in the lungs are not available, the excursion factor of 2 has been retained.

Sensitization. There are still no findings of sensitization of the airways, no clinical findings and only an equivocal result from a maximization test for skin sensitization. Oleoyl sarcosine 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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