1-Ethoxy-2-propyl acetate / 1-Ethoxypropan-2-yl acetate

MAK Value Documentation

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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), the Pregnancy Risk Group and absorption through the skin of 1-ethoxy-2-propyl acetate [54839-24-6].
1-Ethoxy-2-propyl acetate is weakly irritating to the skin and eyes of rabbits. The critical effect is CNS depression after repeated inhalative exposure with a NOAEC of 100 ml/m³ in a 28-day study with rats. Based on this, the maximum concentration at the work place (MAK value) for 1-ethoxy-2-propyl acetate is set at 20 ml/m³ (120 mg/m³). This value also protects against possible irritation, as local effects are not observed up to 1200 ml/m³ in the 28-day rat inhalation study.
Since the critical effect of 1-ethoxy-2-propyl acetate is systemic, Peak Limitation Category II is retained. There are still no specific toxicokinetic data available, so that the default excursion factor of 2 is also retained.
There are no data on reproduction toxicity with 1-ethoxy-2-propyl acetate available. 1-Ethoxy-2-propyl acetate remains assigned to Pregnancy Risk Group C in analogy to 1-ethoxy-2-propanol. On the basis of data with 1-ethoxy-2-propanol and other glycol ether acetates, skin contact is expected to contribute significantly to systemic toxicity and 1-ethoxy-2-propyl acetate is designated with "H".

Keywords

1-ethoxy-2-propyl acetate; 1-ethoxypropan-2-yl acetate; toxicokinetics; metabolism; (sub)acute toxicity; (sub) chronic toxicity; peak limitation; prenatal toxicity; absorption through the skin; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

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1-Ethoxy-2-propyl acetate[1)]

[54839-24-6]

Supplement 2018

MAK value (2017)	**20 ml/m³ (ppm) ≙ 120 mg/m³**
Peak limitation (2006)	**Category II, excursion factor 2**
Absorption through the skin (2017)	**H**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2006)	**Pregnancy Risk Group C**
Germ cell mutagenicity	**–**
BAT value	**not yet established**

Documentation for 1-ethoxy-2-propyl acetate was published in 2007 (documentation "1-Ethoxy-2-propylacetat" 2007, available in German only). In addition, documentation for the BAT value is available (documentation "1-Ethoxy-2-propylacetat" 2009, available in German only); however, a BAT value has not been established.

In 2016, the Commission began using a revised approach for assessing substances with a MAK value based on systemic effects and derived from inhalation studies in animals or studies with volunteers at rest; this new approach takes into account that the respiratory volume at the workplace is higher than under experimental conditions. However, this does not apply to gases or vapour with a blood:air partition coefficient < 5 (see List of MAK and BAT Values). A blood:air partition coefficient of 2701 was calculated for 1-ethoxy-2-propyl acetate using the formula of Buist et al. (2012). This supplement evaluates whether the MAK value and the pregnancy risk group of 1-ethoxy-2-propyl acetate need to be re-assessed as a result of the higher respiratory volume at the workplace.

1) MAK value applies for the sum of the concentrations of 1-ethoxy-2-propanol and 1-ethoxy-2-propyl acetate in the air.

Toxicokinetics and Metabolism

Absorption, distribution, elimination

No experimental data are available for the penetration of 1-ethoxy-2-propyl acetate through the skin. However, the dermal penetration of undiluted 1-ethoxy-2-propanol and a 50% aqueous solution of the substance was determined in human full thickness skin using an in vitro diffusion system. A dose of 200 µl/cm² of the test substance was applied occlusively and the concentration of the test substance in the receptor solution of the diffusion cell was recorded for 8 hours. A dermal flux of 1398 ± 400 µg/cm² and hour was determined after application of undiluted 1-ethoxy-2-propanol, and the dermal flux after application of the 50% aqueous solution was 2133 ± 101 µg/cm² and hour (Korinth et al. 2012).

Subacute, subchronic and chronic toxicity

Inhalation

In a study with 28-day inhalation exposure to 1-ethoxy-2-propyl acetate vapour concentrations of 0, 100, 300 and 1200 ml/m³ for 6 hours per day, on 5 days per week, in whole animal exposure chambers (whole-body exposure), a decreased response to external stimuli was observed in Wistar rats at 300 ml/m³ and above. The decrease in response rapidly disappeared once exposure was discontinued. This effect on the central nervous system (CNS) was detected in the 300 ml/m³ group only at the beginning of exposure; an intensification of the effect was not observed with the increasing exposure period. The chloride levels were significantly increased in the females at concentrations of 300 ml/m³ and above; this effect was not dependent on the concentration (no other details; no individual data are available). Urinalysis was not performed. Substance-induced findings were not reported after gross-pathological and microscopic examination at the end of the study or after organ weights were analysed. A NOAEC (no observed adverse effect concentration) of 100 ml/m³ was determined in the 28-day study (documentation "1-Ethoxy-2-propylacetat" 2007, available in German only).

Manifesto (MAK value/classification)

1-Ethoxy-2-propyl acetate causes slight irritation of the skin and eyes of rabbits. CNS depression is the critical systemic effect after repeated inhalation exposure.

MAK value. The NOAEC after 28-day inhalation exposure of Wistar rats to 1-ethoxy-2-propyl acetate was 100 ml/m³. A decrease in the response to external stimuli without an intensification of the effect over time was observed at concentrations of 300 ml/m³ and above. The chloride levels were significantly increased in the females, but this effect was not dependent on the concentration.

Assuming rapid cleavage of the acetate to form alcohol, in the 2007 documentation (documentation "1-Ethoxy-2-propylacetat" 2007, available in German only)

the MAK value for 1-ethoxy-2-propyl acetate was determined in analogy to the value derived for 1-ethoxy-2-proponal. A 90-day study is available for 1-ethoxy-2-propanol that investigated the effects on Wistar rats exposed to concentrations of 0, 100, 300 and 2000 ml/m^3 for 6 hours per day, on 5 days per week. A decrease in the response to external stimuli was reported at the high concentration, but not at a concentration of 300 ml/m^3. The acetate thus seems to have a slightly stronger effect on the CNS. The urine volume was increased at concentrations of 300 ml/m^3 and above and pale foci were observed in the lungs. There was no effect on chloride levels.

Based on the NOAEC of 100 ml/m^3 for effects on the CNS induced by 1-ethoxy-2-propyl acetate, the extrapolation of the NOAEC from the animal study to humans (1:2), and after taking into consideration the increased respiratory volume of the person at the workplace compared with that of the test animal at rest (1:2) and applying the preferred value approach, a MAK value of 20 ml/m^3 has been established. Observation of this value also provides protection from irritation because local effects were not observed in the 28-day inhalation study up to a concentration of 1200 ml/m^3 and 1-ethoxy-2-propyl acetate was not or was only slightly irritating to the eyes.

Peak limitation. As the MAK value for 1-ethoxy-2-propyl acetate has been derived from systemic effects, this substance remains classified in Peak Limitation Category II. No specific data for the half-life are available. For this reason, the default excursion factor of 2 has been retained.

Prenatal toxicity. The toxic effects of 1-ethoxy-2-propyl acetate on reproduction have not been investigated. In the 2007 documentation (documentation "1-Ethoxy-2-propylacetat" 2007, available in German only), 1-ethoxy-2-propyl acetate was classified in Pregnancy Risk Group C in analogy to 1-ethoxy-2-propanol. The MAK value for 1-ethoxy-2-propanol has been lowered to 20 ml/m^3 and the substance remains classified in Pregnancy Risk Group C (see supplement "1-Ethoxy-2-propanol" 2018). In analogy to 1-ethoxy-2-propanol, 1-ethoxy-2-propyl acetate remains classified in Pregnancy Risk Group C.

Absorption through the skin. In contrast to 1-ethoxy-2-propyl acetate, experimental data are available for the dermal penetration of 1-ethoxy-2-propanol. According to an in vitro study, undiluted 1-ethoxy-2-propanol penetrates the human skin with a flux value of 1398 µg/cm^2 and hour. Comparative analyses of different glycol ethers and their acetates found that the dermal penetration rates of glycol ether acetates are between 10% and 100% of those of the corresponding glycol ethers (Dugard et al. 1984; Larese Filon et al. 1999). Based on the assumption that the penetration rate of 1-ethoxy-2-propyl acetate is lower by a factor of 10, 280 mg of the substance would be absorbed in total after 1-hour exposure of both hands and forearms (approx. 2000 cm^2). Assuming complete absorption and a respiratory volume of 10 m^3, 1200 mg 1-ethoxy-2-propyl acetate would be absorbed by inhalation after 8-hour inhalation exposure at the MAK value (120 mg/m^3). About 25% of the systemically tolerable amount is thus absorbed through the skin. As a result of dermal exposure, observance of the MAK value alone can no longer provide protection from the adverse effects on health that were decisive in determining the thresh-

old value. For this reason, 1-ethoxy-2-propyl acetate retains its "H" designation (for substances which can be absorbed through the skin in toxicologically relevant amounts).

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