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2-Propanol – Addendum: evaluation of a pregnancy risk group for the BAT value

Assessment Values in Biological Material – Translation of the German version from 2023

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Abstract

In 2018, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area re-evaluated and confirmed the maximum workplace concentration (MAK value) of 2-propanol [67-63-0]. If the MAK value of 200 ml 2-propanol/m^3 (500 mg/m^3) is observed, no prenatal toxic effects are to be expected. Therefore, Pregnancy Risk Group C was likewise confirmed. In 2010, biological tolerance values (BAT values) of 25 mg acetone/l blood and 25 mg acetone/l urine were derived in correlation to the MAK value. Pregnancy Risk Group C is therefore similarly valid for the BAT value. In adherence with the BAT values of 25 mg acetone/l blood and 25 mg acetone/l urine, no prenatal toxic effects are to be expected.

BAT value (2009)	**25 mg acetone/l blood** **25 mg acetone/l urine** Sampling time: end of exposure or end of shift
MAK value (1996)	**200 ml/m³ ≙ 500 mg/m³**
Peak limitation (2001)	Category II, excursion factor 2
Prenatal toxicity (1996)	Pregnancy Risk Group C

For 2-propanol, a maximum workplace concentration (MAK value) of 200 ml/m³ (500 ml/m³) was derived with assignment of Pregnancy Risk Group C (Hartwig 2012, 2013; Hartwig and MAK Commission 2019). In 2009, the biological tolerance values (BAT values) were also lowered to 25 mg acetone/l blood and 25 mg acetone/l urine in correlation to the MAK value (Schaller 2021). When setting BAT values, as of 2019, the adoption of the pregnancy risk group valid for the respective MAK value is explicitly verified (DFG 2019). This addendum evaluates whether Pregnancy Risk Group C can similarly be adopted for the BAT values of 2-propanol derived in correlation to the MAK value.

Prenatal toxicity

The available literature on the prenatal toxic effects has been re-evaluated (Hartwig and MAK Commission 2019). Reliable human studies are not available.

Developmental toxicity

Animal studies showed **no teratogenic effects** of 2-propanol in rats and rabbits. In a prenatal developmental toxicity study on rats, only maternally toxic dosages starting at 800 mg/kg body weight yielded observations of reduced foetal weight (Tyl et al. 1994) and postnatal mortality was observed in a one-generation study at concentrations of 2768 mg/kg body weight per day (Faber et al. 2008). After **oral administration**, the **NOAELs** (no observed adverse effect level) for developmental toxicity were 596 mg/kg body weight per day for **rats** (drinking water) and 480 mg/kg body weight per day for **rabbits** (by gavage; maternal toxicity observed as reduced food consumption and body weight gain) (Tyl et al. 1994).

Evaluation of a pregnancy risk group for the BAT Value

From the NOAELs for developmental toxicity for rats of 596 mg/kg body weight per day and for rabbits of 480 mg/kg body weight per day (by gavage) simplified toxicokinetic conversion yielded corresponding air concentrations of 1931 mg/m³ (776 ml/m³) and 2592 mg/m³ (1040 ml/m³), respectively, under consideration of the corresponding species-specific correction values for the toxicokinetic differences between rats or rabbits and humans (1:4 or 2.4), the assumed oral absorption (100%), the experimentally determined inhalation absorption of 54% (Hartwig 2013), the body weight (70 kg), and the respiratory volume (10 m³) of humans.

Using a physiological based pharmacokinetic (PBPK) model (Clewell et al. 2001), an oral dose of 600 mg 2-propanol/kg body weight in rats corresponds to a concentration of about 2000 ml 2-propanol/m³ for an exposure period of 6 hours. The simplified estimation above thus leads to a lower concentration (overestimation of inhalation toxicity). Taking the increased respiratory volume of humans at the workplace into account, the oral NOAEL of about 600 mg/kg body weight per day for rats thereby corresponds to an air concentration of 1000 ml/m³. There is no PBPK model for rabbits. The simplified conversion of the NOAEL for rabbits leads to an air concentration similar to the value calculated from the NOAEL for rats (776 and 1040 ml/m³). Therefore, it can be assumed that the application of a PBPK model using the NOAEL from the rabbit study would also yield a higher workplace air concentration (Hartwig and MAK Commission 2019).

The foetotoxic effects in rats, such as ossification delays (variations), were considered not to be substance-specific, but rather secondarily caused by maternal toxicity. Since no teratogenic effects were observed in rats and rabbits, foetotoxic or toxic effects only arose in offspring in cases of maternal toxicity, and the higher workplace concentration calculated with the PBPK model lead to an increased margin between the converted NOAEL for developmental toxicity and the MAK value (5-fold margin), the assignment of 2-propanol to Pregnancy Risk Group C was confirmed (Hartwig 2012; Hartwig and MAK Commission 2019).

Based on the available data, prenatal toxic effects are not expected for exposure at the level of the MAK value of 200 ml 2-propanol/m^3 (500 mg/m^3) and 2-propanol has therefore been assigned to Pregnancy Risk Group C. Since the BAT values were derived in correlation to the MAK value,

prenatal toxic effects are not to be expected,
if the BAT values for 2-propanol of 25 mg acetone/l blood and 25 mg/acetone/l urine are not exceeded.

Notes

Competing interests

The established rules and measures of the commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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