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Isopropylbenzene – 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 2012, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area re-evaluated the maximum workplace concentration (MAK value) of isopropylbenzene (cumene) [98-82-8]. If the MAK value of 10 ml isopropylbenzene/m^3 (50 mg/m^3) is observed, no prenatal toxic effects are to be expected. Therefore, Pregnancy Risk Group C was confirmed. In 2013, the biological tolerance value (BAT value) of 10 mg 2-phenyl-2-propanol (after hydrolysis)/g creatinine was derived in correlation to the MAK value. Pregnancy Risk Group C is also similarly valid for the BAT value. In adherence with the BAT value of 10 mg 2-phenyl-2-propanol (after hydrolysis)/g creatinine, no prenatal toxic effects are to be expected.

BAT value (2013)	**10 mg 2-phenyl-2-propanol (after hydrolysis)/g creatinine** Sampling time: end of exposure or end of shift
MAK value (2012)	**10 ml/m³ ≙ 50 mg/m³**
Peak limitation (2002)	Category II, excursion factor 4
Absorption through the skin (1966)	H
Carcinogenicity (2012)	Category 3
Prenatal toxicity (1996)	Pregnancy Risk Group C

In 2012, the maximum workplace concentration (MAK value) for isopropylbenzene was lowered to 10 ml/m³ (50 mg/m³) and its assignment to Pregnancy Risk Group C was confirmed (Jahnke et al. 2016). In 2013, a biological tolerance value (BAT value) of 10 mg 2-phenyl-2-propanol (after hydrolysis)/g creatinine was derived in correlation to the MAK value (Klotz and Knecht 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 value of isopropylbenzene.

Prenatal toxicity

The available literature on the prenatal toxic effects of isopropylbenzene has been re-evaluated (Jahnke et al. 2016). Reliable human studies are not available.

Developmental toxicity

Comprehensive details on the **developmental toxicity** of isopropylbenzene can be found in Greim (1999), Jahnke et al. (2016), and Hartwig and MAK Commission (2018).

In prenatal developmental toxicity studies according to OECD Test Guideline 414, no embryotoxic or foetotoxic effects in any concentration group arose in Sprague-Dawley **rats** following **inhalation exposure** to 0, 100, 500, or 1200 ml isopropylbenzene/m³ for 6 hours per day from day 6 to day 15 of gestation. The incidence of malformations did not differ from the control value. The NOAEC (no observed adverse effect concentration) for maternal toxic effects was 100 ml/m³ and that for reproductive toxicity 1200 ml/m³ (CMA 1989 a). White New Zealand **rabbits** exhibited maternal toxicity following **inhalation exposure** to 0, 500, 1200, and 2300 ml isopropylbenzene/m³ for 6 hours per day from day 6 to day 18 of gestation at the lowest concentration and above. Embryotoxic and foetotoxic effects did not arise in any concentration group. The increase in the number of offspring with subcutaneous haemorrhages on the head was statistically significant in the 500 ml/m³ group. The incidence of malformations was not different from that of the control group; the incidences for the skeletal variations unilateral, rudimentary thirteenth rib and bilateral, rudimentary third rib, were even reduced in the high-concentration groups compared to the controls (CMA 1989 b). The subcutaneous haemorrhages were considered by the Commission to be irrelevant for the evaluation of developmental toxicity (Greim 1999). In these studies, isopropylbenzene thus proved not to be teratogenic to rats and rabbits.

Evaluation of a pregnancy risk group for the BAT value

Animal studies showed no foetotoxic or teratogenic effects **following inhalation exposure** of **rats** and **rabbits** up to maternally toxic concentrations of 1200 or 2300 ml isopropylbenzene/m³. The NOAEC for prenatal developmental toxicity was 1200 ml isopropylbenzene/m³. Since there is, even considering the increased respiratory volume at the workplace (1:2), a sufficiently large 60- or 115-fold margin between the NOAEC for developmental toxicity and the MAK value, isopropylbenzene is assigned to **Pregnancy Risk Group C**.

Based on the available data, prenatal toxic effects are not to be expected for exposure at the level of the MAK value of 10 ml isopropylbenzene/m^3 (50 mg/m^3) and isopropylbenzene is assigned to Pregnancy Risk Group C. Since the BAT value for isopropylbenzene was derived in correlation to the MAK value,

prenatal toxic effects are not to be expected,
if the BAT value of 10 mg 2-phenyl-2-propanol (after hydrolysis)/g creatinine is 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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