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1,4-Dioxane – Addendum: evaluation of a pregnancy risk group for the BAT value

Assessment Values in Biological Material – Translation of the German version from 2022

W. Weistenhöfer[1]
S. Michaelsen[2]
G. Schriever-Schwemmer[2]
H. Drexler[3,*]
A. Hartwig[4,*]
MAK Commission[5,*]

1 *Friedrich-Alexander-Universität Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Henkestraße 9–11, 91054 Erlangen, Germany*

2 *Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

3 *Head of the working group "Assessment Values in Biological Material" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Friedrich-Alexander-Universität Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Henkestraße 9–11, 91054 Erlangen, Germany*

4 *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*

5 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: H. Drexler (hans.drexler@fau.de), A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

Keywords

1,4-dioxane; biological tolerance value; BAT value; developmental toxicity; prenatal toxicity

Abstract

In 2018, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the maximum workplace concentration (MAK value) of 1,4-dioxane [123-91-1]. If the MAK value of 10 ml 1,4-dioxane/m^3 (37 mg/m^3) is not exceeded, prenatal toxic effects are not to be expected, so that Pregnancy Risk Group C was confirmed. In 2019, the biological tolerance value (BAT value) of 200 mg 2-hydroxyethoxyacetic acid/g creatinine was derived in correlation to the MAK value. Therefore, Pregnancy Risk Group C is also valid for the BAT value. Adhering to the BAT value of 200 mg 2-hydroxyethoxyacetic acid/g creatinine, prenatal toxic effects are not to be expected.

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BAT value (2019)	**200 mg 2-hydroxyethoxyacetic acid/g creatinine** Sampling time: end of exposure or end of shift
MAK value (2018)	**10 ml/m³ ≙ 37 mg/m³**
Peak limitation (2018)	Category I, excursion factor 2
Absorption through the skin (1966)	H
Carcinogenicity (1998)	Category 4
Prenatal toxicity (2006)	Pregnancy Risk Group C

In 2018, a maximum workplace concentration (MAK value) of 10 ml/m³ (37 mg/m³) was derived for 1,4-dioxane and Pregnancy Risk Group C was confirmed (translated in Hartwig and MAK Commission 2020). In 2019, a biological tolerance value (BAT value) of 200 mg 2-hydroxyethoxyacetic acid/g creatinine was derived in correlation to the MAK value (translated in Eckert et al. 2020). When deriving BAT values, since 2019 the adoption of the pregnancy risk group derived for the respective MAK value is explicitly checked (DFG 2019). This addendum evaluates whether Pregnancy Risk Group C can be adopted also for the BAT value of 1,4-dioxane.

Prenatal toxicity

The available literature on the prenatal toxic effects of 1,4-dioxane has been re-evaluated (Hartwig and MAK Commission 2020). Reliable studies in humans are not available.

In developmental toxicity studies with 1,4-dioxane as a stabiliser for 1,1,1-trichloroethane, no developmental toxic effects occurred in **rats** and **mice** after **inhalation** exposure up to the highest concentration of 32 ml 1,4-Dioxan/m³ (Schwetz et al. 1975). Likewise, no developmental toxic effects were observed in Sprague Dawley **rats** in a **drinking water study** with administration of 0.9 mg 1,4-dioxane/l drinking water (0.1 mg 1,4-dioxane/kg body weight and day) (George et al. 1989).

In a prenatal developmental toxicity study in **rats**, reduced body weight gains of the dams and decreased body weights of the foetuses but no teratogenic effects were found after **gavage** of 1035 mg 1,4-dioxane/kg body weight and day (Giavini et al. 1985). The NOAEL (no observed adverse effect level) for developmental and maternal toxicity in this study was 520 mg 1,4-dioxane/kg body weight and day. After toxicokinetic extrapolation of the NOAEL for developmental toxicity, a 1,4-dioxane concentration in workplace air of 1520 mg/m³ is calculated which is 41-fold to the MAK value of 37 mg/m³. The sufficiently large difference together with the absence of teratogenic effects confirms the assignment of 1,4-dioxane to Pregnancy Risk Group C (Hartwig and MAK Commission 2020).

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 1,4-dioxane/m³ (37 mg/m³). 1,4-Dioxane has therefore been assigned to Pregnancy Risk Group C. Since the BAT value was derived in correlation to the MAK value,

prenatal toxic effects are not to be expected,
if the BAT value of 200 mg 2-hydroxyethoxyacetic acid/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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