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Dichloromethane – 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 2014, 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 dichloromethane [75-09-2] and set a MAK value of 50 ml dichloromethane/m^3 (180 mg/m^3). In humans, exposure to 50 ml/m^3 of dichloromethane led to CO-Hb levels in the range of 3%, which is above the endogenous CO-Hb range of 0.4–2.6% in non-smoking pregnant women. There is no information available on the CO-Hb level at which oxygen deficiency occurs in the foetal tissues. As a result, the possibility of prenatal toxicity cannot be excluded even if the MAK value of 50 ml dichloromethane/m^3 is observed. Based on this finding, classification in Pregnancy Risk Group B has been confirmed. In 2015, the biological tolerance value (BAT value) of 500 µg dichloromethane/l blood was derived in correlation to the MAK value. Pregnancy Risk Group B is therefore also valid for the BAT value. The possibility of prenatal toxicity cannot be excluded even when adhering to the BAT value of 500 µg dichloromethane/l blood.

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BAT value (2015)	**500 µg dichloromethane/l blood** Sampling time: immediately after exposure
MAK value (2014)	**50 ml/m³ ≙ 180 mg/m³**
Peak limitation (2014)	Category II, Excursion factor 2
Absorption through the skin (2014)	H
Carcinogenicity (2014)	Category 5
Prenatal toxicity (2014)	Group B

In 2014, a maximum workplace concentration (MAK value) of 50 ml/m³ (180 mg/m³) (due to neurotoxic effects and the formation of CO-Hb) as well as an assignment to Pregnancy Risk Group B was established for dichloromethane (translated in Hartwig and MAK Commission 2016). In humans, exposure to 50 ml dichloromethane/m³ leads to CO-Hb levels in the range of 3%. In 2015, a biological tolerance value (BAT value) of 500 µg dichloromethane/l blood was derived in correlation to the MAK value (translated in Bolt et al. 2018). 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 B can similarly be adopted for the BAT value of dichloromethane.

Prenatal toxicity

Human data have to be used when evaluating prenatal toxicity, as humans react more sensitively to neurotoxicity compared to animals, and, in terms of neurotoxicity, a foetus is at least as susceptible as an adult. Due to the insufficient data on developmental toxicity and developmental neurotoxicity in humans, dichloromethane would be assigned to Pregnancy Risk Group D.

Carbon monoxide, which has been assigned to Pregnancy Risk Group B, is a metabolite of dichloromethane (translated in Henschler 1992). Endogenous formation of CO is increased by a factor of 1.5–3 in pregnant women compared to non-pregnant women. Non-smoking pregnant women have an average CO-Hb value of 0.4–2.6%, whereas this value is 0.4–1.1% in non-pregnant women (Longo 1970).

Carbon monoxide can cross the placenta whereby increased CO-Hb levels and the resulting O_2 deficiency may lead to such foetal effects as reduced birth weight and an increased heart rate. In equilibrium conditions, the proportion of CO-Hb in foetal blood is somewhat higher than that of the mother's blood. The foetal CO-Hb value exhibits a delayed increase over several hours and is 10 to 15% higher than that of the mother (Astrup et al. 1972; Longo 1970). Since foetal effects above the maximum endogenous CO-Hb value for pregnant women (CO-Hb value up to 2.6%), even at exposures at the level of the MAK value of dichloromethane (CO-Hb value of 3%), could not be ruled out, dichloromethane like its metabolite carbon monoxide has been assigned to Pregnancy Risk Group B.

Evaluation of a pregnancy risk group for the BAT value

Workplace exposure to 50 ml dichloromethane/m³ leads to a CO-Hb value in the range of 3% (Soden et al. 1996), which is above the endogenous CO-Hb value of 0.4–2.6% in non-smoking pregnant women. Since no information is available as to which CO-Hb level results in oxygen deficiency in foetal tissues, the possibility of foetal effects cannot be excluded at a CO-Hb value of about 3%, and dichloromethane is therefore assigned to Pregnancy Risk Group B. As the BAT value for dichloromethane was derived in correlation to the MAK value of 50 ml dichloromethane/m³,

the possibility of prenatal effects cannot be excluded
by compliance with the BAT value of 500 µg dichloromethane/l blood.

Since the CO-Hb value itself is subject to variations and since exposures other than dichloromethane, such as smoking, may add to the CO-Hb level and cannot be controlled, the derivation of a NOAEC (no observed adverse effect concentration) for maternal CO-Hb entails too much uncertainty. For this reason, no information can be given on the prerequisite for classification in Pregnancy Risk Group C (Hartwig and MAK Commission 2016).

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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