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N,N-Dimethylacetamide – Addendum: evaluation of the pregnancy risk group for the BAT value

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

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Abstract

In 2017, 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 *N,N*-dimethylacetamide [127-19-5]. If the MAK value of 5 ml *N,N*-dimethylacetamide/m^3 (18 mg/m^3) is not exceeded, prenatal toxic effects are not to be expected and Pregnancy Risk Group C was confirmed. In 2019, the biological tolerance value (BAT value) of 25 mg *N*-methylacetamide plus *N*-hydroxymethyl-*N*-methylacetamide/l urine 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 25 mg *N*-methylacetamide plus *N*-hydroxymethyl-*N*-methylacetamide/l urine, prenatal toxic effects are not to be expected.

BAT value (2019)	**25 mg *N*-methylacetamide plus *N*-hydroxymethyl-*N*-methylacetamide/l urine** Sampling time: end of exposure or end of shift; at the end of shift, for long-term exposures after several previous shifts
MAK value (2017)	**5 ml/m³ ≙ 18 mg/m³**
Peak limitation (2002)	Category II, excursion factor 2
Absorption through the skin (1969)	H
Carcinogenicity	–
Prenatal toxicity (1990)	Pregnancy Risk Group C

In 2017, a maximum workplace concentration (MAK value) of 5 ml/m³ (18 mg/m³) was derived for *N,N*-dimethylacetamide and Pregnancy Risk Group C was confirmed (translated in Hartwig and MAK Commission 2019). The substance can be absorbed through the skin both in liquid form and from the gaseous phase (Greim 1998). In 2019, a biological tolerance value (BAT value) of 25 mg *N*-methylacetamide plus *N*-hydroxymethyl-*N*-methylacetamide/l urine was derived in correlation to the MAK value (translated in Walter 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 also be adopted for the BAT value of *N,N*-dimethylacetamide.

Prenatal toxicity

The available literature on the prenatal toxic effects of *N,N*-dimethylacetamide has been re-evaluated (Hartwig and MAK Commission 2019). In 1990, *N,N*-dimethylacetamide was classified in Pregnancy Risk Group C. This classification was confirmed in 1998 provided skin contact is avoided (Greim 1998). Reliable studies in humans are not available.

In a **gavage study** in **rats**, the NOAEL (no observed adverse effect level) for developmental and maternal toxicity was 65 mg *N,N*-dimethylacetamide/kg body weight. In rats given 150 mg *N,N*-dimethylacetamide/kg body weight and day, one foetus showed malformations (DuPont 1997), therefore this dose is interpreted as the lower end of the dose–response relationship for malformation. The 15-fold margin to the MAK value given at this dose is considered to be sufficiently large, especially since the NAEL based on the marginal effects like reduced body weight could even be higher than 65 mg/kg body weight and day and the inhalation study in rats relevant for the workplace yielded a sufficiently large difference of the NOAEC (no observed adverse effect concentration) of 300 ml/m³ to the MAK value.

In the **inhalation study** in **rabbits**, the NOAEC (no observed adverse effect concentration) and LOAEC (lowest observed adverse effect concentration) for additional ribs, a skeletal variation, were 57 and 200 ml *N,N*-dimethylacetamide/m³, respectively, without maternal toxicity (Klimisch and Hellwig 2000). This effect is an incipient marginal effect, the NAEC could therefore likewise be higher in this case and the margin to the MAK value would then be more than 6-fold.

In the other animal studies with inhalation exposure to and oral administration of *N,N*-dimethylacetamide, the differences of the calculated NOAECs for developmental toxicity and perinatal toxicity to the MAK value were sufficiently large. For these reasons, the assignment of *N,N*-dimethylacetamide to Pregnancy Risk Group C was confirmed (Hartwig and MAK Commission 2019).

Based on the available data, prenatal toxic effects are not to be expected for exposure at the level of the MAK value of 5 ml *N*,*N*-dimethylacetamide/m^3 (18 mg/m^3). *N*,*N*-Dimethylacetamide 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 25 mg *N*-methylacetamide plus *N*-hydroxymethyl-*N*-methylacetamide/l urine 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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