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N,N-Dimethylacetamide – Addendum for re-evaluation of the BAT value

Assessment Values in Biological Material – Translation of the German version from 2020

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Abstract

In 2019, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the BAT value of N,N-dimethylacetamide [127-19-5], following the re-evaluation of the MAK value.

The major routes of uptake of N,N-dimethylacetamide in the workplace are inhalation and nearly 30% dermal absorption. Several studies indicated a non-linear correlation between occupational exposure and urinary excretion of N-methylacetamide. An equation for the correlation between occupational exposure to N,N-dimethylacetamide in air and urinary excretion of N-methylacetamide was reported, which is in line with the results of field and human exposure studies. The equation does not consider the additional dermal uptake of liquid N,N-dimethylacetamide. In correlation to the MAK value of 5 mg N,N-dimethylacetamide/m^3, a BAT value of 25 mg N-methylacetamide plus N-hydroxymethyl-N-methylacetamide/l urine was established. Sampling time is at the end of exposure or end of shift. Sampling time for long-term exposures is at the end of the shift after several shifts.

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BAT value (2019)	**25 mg N-methylacetamide plus N-hydroxymethyl-N-methylacetamide/l urine** Sampling time: end of exposure or end of shift; for long-term exposure: at the end of the shift after several shifts
MAK value (2017)	**5 ml/m³ ≙ 18 mg/m³**
Absorption through the skin (1969)	H
Carcinogenicity	–

Re-evaluation

For substances whose MAK value is based on systemic effects and was derived from animal inhalation studies or studies involving volunteers at rest, the Commission has taken into account since 2016 that the respiratory volume in the workplace is higher than under these experimental conditions (Hartwig and MAK Commission 2017). However, this does not apply to gases and vapours if their blood:air partition coefficient is < 5 (see List of MAK and BAT Values, DFG 2019). The blood:air partition coefficient for N,N-dimethylacetamide calculated according to the formula developed by Buist et al. (2012) is 26 037. Taking into account the increased respiratory volume in the workplace, the MAK value of N,N-dimethylacetamide was reduced from 10 ml/m³ to 5 ml/m³ (Hartwig and MAK Commission 2019).

The dermal intake of N,N-dimethylacetamide in humans from the gas phase is particularly high. Consequently, the concentration of the urinary metabolite N-methylacetamide results from 70% inhalation and 30% percutaneous (vapour) absorption of N,N-dimethylacetamide from the air (Maxfield et al. 1975). According to Nomiyama et al. (2000), dermal absorption of vaporous N,N-dimethylacetamide accounts for about 40% of the N-methylacetamide excreted in urine.

Kennedy and Pruett (1989) as well as Borm et al. (1987) have described a non-linear relationship between the concentration of N,N-dimethylacetamide in air and N-methylacetamide in urine. Kennedy (1990) derived from his data (Kennedy and Pruett 1989) and the study by Borm et al. (1987) the following equation for the non-linear relationship between exposure to N,N-dimethylacetamide (DMAC) in air and the concentration of N-methylacetamide (NMAC) in urine:

$$\mathbf{NMAC}\,[\mathbf{mg/l\,urine}] = \frac{\mathbf{37.8} \times \mathbf{17} \times \mathbf{DMAC}\,[\mathbf{ml/m^3}]}{\mathbf{37.8} + (\mathbf{17} \times \mathbf{DMAC}\,[\mathbf{ml/m^3}])}$$

Table 1 shows the N-methylacetamide concentrations in urine calculated according to Kennedy (1990) after end of shift for N,N-dimethylacetamide concentrations in air of 1, 5 and 10 ml DMAC/m³.

Tab. 1 N,N-Dimethylacetamide concentrations in air and N-methylacetamide concentrations in urine after end of shift (calculation according to Kennedy 1990)

N,N-dimethylacetamide in air [ml/m³]	N-methylacetamide in urine [mg/l]
10	31
5	26
1	12

Based on the MAK value of 5 ml N,N-dimethylacetamide/m³ in air, the equation of Kennedy (1990) yields a N-methylacetamide concentration in urine of 26 mg/l.

Hence, a **BAT value** of

25 mg N-methylacetamide/l urine

is established. The sampling time is at the end of exposure or end of shift, for long-term exposures: at the end of the shift after several shifts.

The BAT value relates to normally concentrated urine, in which the creatinine level should be in the range between 0.3 and 3 g/l. It is generally recommended that the measurement be repeated in normally hydrated subjects if urine samples are outside the above-mentioned limits (Bader et al. 2016).

As already stated in the BAT addendum of 2010 (translated in Bader 2016), to determine the N-methylacetamide in urine, the sum of N-methylacetamide and the dimethylacetamide metabolites N-hydroxymethyl-N-methylacetamide are analysed using gas chromatography. In the injector of the gas chromatograph, N-hydroxymethyl-N-methylacetamide cleaves off formaldehyde and forms N-methylacetamide. The current BAT value accounts for this reaction and is related to the sum of N-methylacetamide excreted in urine and that formed in the injector (Knecht and Müller 2003).

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