

Vinyl chloride – Addendum: Re-evaluation of the BAR

Assessment Values in Biological Material – Translation of the German version from 2023

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Abstract

In 2022, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has withdrawn the exposure equivalents for carcinogenic substances (EKA) for vinyl chloride [75-01-4] based on urinary excretion of thiodiglycolic acid (TdAA) because of its poor reliability at low exposure. Therefore, also the biological reference value (BAR) has to be re-evaluated. To this end, the existing literature was updated and taken into account. Four published studies showed that the excretion of TdAA in humans occupationally exposed to vinyl chloride and non-exposed persons largely overlaps, especially in the exposure range $< 5 \text{ ml/m}^3$. This may lead to a situation where unexposed persons may falsely be considered exposed to vinyl chloride as well as – on the other hand – real exposures may not be identified. Nevertheless, in order to keep an instrument for the assessment of higher exposures, notably after accidents or leakages, the Commission decided to confirm the existing BAR of 1.5 mg TdAA/l urine, however with the additional remark “This BAR is not suitable for the assessment of vinyl chloride exposures $< 5 \text{ ml/m}^3$ ”. Owing to the different excretion characteristics after high vs. low vinyl chloride exposures it is further recommended to obtain two separate urine samples after 12–18 and 48 hours, respectively, after an accidental exposure.

Citation Note:

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EKA (2021)	not established
BAR (2009)	1.5 mg thiodiglycolic acid/l urine^{a)} Sampling time: at the beginning of the next shift
MAK value	–
Carcinogenicity (1977)	Category 1

^{a)} The BAR for TdAA is not suitable for the assessment of vinyl chloride exposures < 5 ml/m³.

Re-evaluation

For vinyl chloride, exposure equivalents for carcinogenic substances (EKA) were derived in 1989 (translated in Müller and Norpoth 1995), confirmed in 2009 and supplemented by a biological reference value (BAR) (translated in Kraus et al. 2016). The main quantitative metabolite thiodiglycolic acid (thiodiacetic acid, TdAA) was selected as the parameter for assessing exposure. However, TdAA is formed in the metabolism from a whole series of C2-alkylants and is also formed physiologically, so that this parameter can be considered neither particularly sensitive nor specific (Müller and Norpoth 1995).

For the derivation of EKA, the TdAA concentration in the 24-hour urine should be determined after the start of the shift. However, since the collection of 24-hour urine is difficult to organise from a practical point of view and prone to errors, the available data for the derivation of EKA based on TdAA concentrations in spontaneous urine samples were reviewed, and recent study results were taken into account. The correlation between vinyl chloride exposure and TdAA excretion, especially in the practically relevant exposure range below 5 ml/m³, turned out not to be sufficiently reliable. Therefore, the EKA have been withdrawn (Nasterlack et al. 2022). Against this background, it has become necessary to review the BAR for vinyl chloride.

Re-evaluation of the BAR for vinyl chloride

In 2009, the BAR for vinyl chloride was set at 1.5 mg TdAA/l urine. Sampling should take place at the beginning of the shift following exposure. A study by Müller et al. (1979) was used as a basis, which was carried out in persons who had not been exposed to vinyl chloride or other substances known to be metabolised to TdAA. The mean values for men and women were 0.67 ± 0.32 and 0.51 ± 0.02 mg TdAA/l urine, respectively. The 99th percentiles were 1.82 and 1.43 g TdAA/l urine, respectively.

Chen et al. (1983) reported a mean value for TdAA excretion of 0.83 ± 0.56 mg/l urine (maximum 2.4 mg/l) in 78 non-exposed persons, which is approximately in the order of magnitude reported by Müller et al. (1979). Up to the maximum value of 2.4 mg TdAA/l urine, which was reached several times also by non-exposed persons, there was a clear overlap with the exposed persons.

In the study by Shayakhmetov et al. (2019), TdAA concentrations were determined in the urine of 65 employees from vinyl chloride and polyvinyl chloride production departments (sampling 15 to 64 hours after the last exposure), 10 shift workers in the polyvinyl chloride production department (sampling at the end of the shift and before the start of the next shift) and 34 employees not exposed to chemicals as control subjects. The background exposure of the non-exposed control subjects was reported to be 0.27 ± 0.13 mg TdAA/l urine on average, which is significantly lower than that reported by Müller et al. (1979). Despite the fact that the background exposure was comparatively low, it was not exceeded by 9% of the vinyl chloride production workers and by 26% of the polyvinyl chloride workers.

The BAR can also be compared with the findings of Cheng et al. (2001) in 16 workers exposed to vinyl chloride in PVC production. Here, 12 of the workers were exposed to concentrations of less than 5 ml/m³. In this study, 3 of 16 post-shift urine samples from individuals with time-weighted vinyl chloride exposures of 0.25, 0.68 and 4.86 ml/m³ were within

the background exposure range. In the samples taken before the start of the shift on the following day, this was the case for 4 out of 16 samples, one of which was from a person whose exposure value on the previous day was 3.39 ml/m³.

Re-evaluation of the BAR for the parameter TdAA

From the available data it can be deduced that the reliability of the parameter TdAA to discriminate between exposed and non-exposed persons in a vinyl chloride exposure range below 5 ml/m³ is very poor. This may lead to a situation where unexposed persons may falsely be considered vinyl chloride-exposed as well as – on the other hand – real exposures may not be identified. This limitation should be borne in mind when applying the BAR to assess situations of operational routine.

In practice, however, it is helpful to be able to assess higher exposures, notably after leakages or accidents. As the time of the maximum of TdAA excretion can vary considerably depending on the exposure level, it is recommended in such cases to examine at least two urine samples. These should be obtained about 12 to 18 and 48 hours after the accident.

Based on the available data, the

BAR for vinyl chloride of 1.5 mg TdAA/l urine

is confirmed with the remark “This BAR is not suitable for the assessment of vinyl chloride exposures < 5 ml/m³”. Sampling time is at the beginning of the next shift. After accidental exposures, a second urine sample should be obtained 48 hours after the accident.

Interpretation

The BAR refers to normally concentrated urine in which the creatinine content should be in the range of 0.3–3.0 g/l. In cases of urine samples outside the above limits, it is generally recommended to repeat analysis with normally hydrated test persons (translated in Bader et al. 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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