The MAK-Collection for Occupational Health and Safety

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1,2-Epoxypropane – Addendum for evaluation of a BAT value

Assessment Values in Biological Material – Translation of the German version from 2015

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1,2-epoxypropane, propylene oxide, BAT value, biological tolerance value, biomonitoring, N-(2-hydroxypropyl)valine, 2-hydroxypropyl mercapturic acid

BAT value (2014)

2500 pmol *N*-(2-Hydroxypropyl)valine/g globin (erythrocyte fraction of whole blood)
Sampling time: not fixed[a)]

EKA (2012)

The following correlation between external and internal exposure was established:

Air		Erythrocyte fraction of whole blood
1,2-Epoxypropane		*N*-(2-Hydroxypropyl)valine
[ml/m³]	[mg/m³]	[pmol/g globin]
0.5	1.2	600
1.0	2.4	1300
2.0	4.8	2600
2.5	6.0	3200

Sampling time: not fixed[a)]

BAR (2011)

10 pmol *N*-(2-Hydroxypropyl)valine/g globin[b)]
Sampling time: not fixed[a)]

25 µg 2-Hydroxypropyl mercapturic acid/g creatinine[b)]
Sampling time: end of exposure or end of shift; for long-term exposures: at the end of the shift after several previous shifts

MAK value (2012)

2 ml/m³ (ppm) ≙ 4.8 mg/m³

Absorption through the skin

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Carcinogenicity (2012)

Category 4

[a)] changed to "sampling time: after exposure for at least 3 months" in 2016 (DFG 2016)

[b)] evaluated for non-smokers

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Re-evaluation

In 2011, biological reference values (BAR) of 10 pmol *N*-(2-hydroxypropyl)valine/g globin and 25 µg 2-hydroxypropyl mercapturic acid/g creatinine were derived for 1,2-epoxypropane [75-56-9] for non-smokers (translated in Bader et al. 2016). EKA (exposure equivalents for carcinogenic substances) were published in 2012 (translated in Bader 2021).

The MAK value (maximum workplace concentration) for 1,2-epoxypropane was re-evaluated in 2012 (translated in Hartwig 2015). In the light of more recent studies on its metabolism, carcinogenicity and genotoxicity, the substance was reclassified from Carcinogen Category 2 into Category 4. In addition, a MAK value of 2 ml 1,2-epoxypropane/m^3 was derived based on a LOAEC (lowest observed adverse effect concentration) of 30 ml 1,2-epoxypropane/m^3 for histopathological changes in the nasal turbinates observed in a 28-day study in rats and on a corresponding BMDL05 (lower 95% confidence limit of an incidence increase by 5%) of 11 ml 1,2-epoxypropane/m^3 using a PBPK model. Following this reclassification and the establishment of a MAK value, it should be assessed whether the already existing EKA can be used to derive a health-based biological tolerance value (BAT value).

Exposure and Effects

Relationship between external and internal exposure

The EKA is based on investigations by Boogaard et al. (1999). In a field study, the authors investigated the relationship between the concentration of 1,2-epoxypropane in air and the concentration of the protein adduct *N*-(2-hydroxypropyl)valine (HPV) in blood. In this case, shift-related measurements of the concentration of 1,2-epoxypropane in air were carried out among 15 of 27 workers during a maintenance shutdown and revision. In 80% of all measurements (89 of 112) the concentration of airborne 1,2-epoxypropane was below the detection limit of the method used (0.08 ml/m^3). The average external exposure was 0.33 ml 1,2-epoxypropane/m^3, the maximum value was 4.1 ml 1,2-epoxypropane/m^3. A biomonitoring survey prior to the maintenance activities revealed an average HPV concentration in blood of 40.2 ± 8.0 pmol/g globin (median: 24.4 pmol/g globin). After the maintenance works were completed, the average value of HPV was increased to 45.3 ± 8.0 pmol/g globin (median: 45.7 pmol/g globin). A complete exposure profile could be established for 13 persons throughout the period of their activities. From these data, the cumulative external exposure was calculated and correlated to the increase in HPV concentrations prior to and after the maintenance shutdown (Boogaard et al. 1999).

Evaluation of the BAT value

The concentrations of 1,2-epoxypropane in air reported by Boogaard et al. (1999) are on average one sixth of the MAK value. In individual cases, however, exposure peaks up to double the MAK value were determined and used for the calculations. The study of Boogaard et al. (1999) appears therefore suitable for the derivation of a BAT value. From the quantitative relationship between the concentration of 1,2-epoxypropane in air and the concentration of *N*-(2-hydroxypropyl)valine in blood as determined by the authors, an HPV concentration of 2600 pmol/g globin is obtained for an 8-hour working day exposure to 2 ml 1,2-epoxypropane/m^3. By rounding,

a BAT value of 2500 pmol *N*-(2-hydroxypropyl)valine/g globin (erythrocyte fraction of whole blood)

is derived. The BAT value is based on the MAK value of 2 ml/m^3 (Hartwig 2015) and applies to an exposure under steady-state conditions, i.e. in the case of the haemoglobin adducts after a representative total working period of 120 days. Where appropriate, the fact that exposure peaks are not reflected in the determination of the adduct levels must be given special consideration, because it means that a continuous exposure lasting 120 days can lead

to the same adduct values as occasional exposure peaks. Owing to the long half-life of the adduct level, there is no fixed sampling time required.

Note: The sampling time was changed to "after exposure for at least 3 months" in 2016 (DFG 2016).

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

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