

1,2-Epoxypropane – 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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Keywords

1,2-epoxypropane; biological tolerance value; BAT value; developmental toxicity; prenatal toxicity; pregnancy risk group

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Abstract

Citation Note:

Weistenhöfer W, Michaelsen S, Schriever-Schwemmer G, Drexler H, Hartwig A, MAK Commission. 1,2-Epoxypropane – Addendum: evaluation of a pregnancy risk group for the BAT value. Assessment Values in Biological Material – Translation of the German version from 2023. MAK Collect Occup Health Saf. 2023 Sep;8(3):Doc069. https://doi.org/10.34865/bb7556e8_3ad

In 2012, 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 1,2-epoxypropane (propylene oxide) [75-56-9]. If the MAK value of 2 ml 1,2-epoxypropane/m³ (4.8 mg/m³) is observed, no prenatal toxic effects are to be expected. 1,2-epoxypropane was therefore classified in Pregnancy Risk Group C. In 2014, the biological tolerance value (BAT value) of 2500 pmol N-(2-hydroxypropyl)valine/g globin was derived in correlation to the MAK value. As a result, Pregnancy Risk Group C is likewise valid for the BAT value. No prenatal toxic effects are to be expected by compliance with the BAT value of 2500 pg N-(2-hydroxypropyl)valine/g globin.

Manuscript completed:
21 Sep 2022

Publication date:
29 Sep 2023

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BAT value (2014)	2500 pmol N-(2-hydroxypropyl)valine/g globin (erythrocyte fraction of whole blood) Sampling time: after exposure for at least 3 months
MAK value (2012)	2 ml/m³ ≅ 4.8 mg/m³
Peak limitation (2012)	Category I, Excursion factor 2
Carcinogenicity (2014)	Category 4
Absorption through the skin	–
Sensitization (2012)	Sh
Prenatal toxicity (2012)	Group C

In 2012, a maximum workplace concentration (MAK value) of 2 ml/m³ (4.8 mg/m³) as well as an assignment to Pregnancy Risk Group C was established for 1,2-epoxypropane (translated in Hartwig 2015). In 2014, in correlation to the MAK value, a biological tolerance value (BAT value) of 2500 pmol N-(2-hydroxypropyl)valine/g globin was derived for the erythrocyte fraction of whole blood (translated in Bader 2021). When setting the 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 C can similarly be adopted for the BAT value of 1,2-epoxypropane.

Prenatal toxicity

The available literature on prenatal toxic effects has been evaluated (Hartwig 2015). Reliable human studies are not available.

In a two-generation study similar to OECD Test Guideline 416 in which 30 male and 30 female Fischer 344 rats were exposed to 1,2-epoxypropane at concentrations of 0, 30, 100, or 300 ml/m³, the high-concentration group of the F1 generation exhibited a statistically significant body-weight reduction of 12% in both genders. No effects were observed on the mating and fertility index, litter size, or on the number of living offspring on the day of birth as well as on postnatal days 4 and 28. Histological investigations showed no effects in the F1 and F2 offspring (Hayes et al. 1988). In a prenatal developmental toxicity study following OECD Test Guideline 414, a statistically significant inhibition of maternal body weight development as well as reduced food consumption was determined in the highest concentration group after inhalation exposure of Fischer 344 rats from day 6–15 of gestation to 0, 100, 300, or 500 ml/m³ 1,2-epoxypropane for 6 hours per day. No adverse effects on litter size, foetal resorption, or foetal weight were observed. The incidence of length variants of the seventh cervical rib was increased in foetuses of the highest concentration group (13%) compared with the control group (2.8%) (Harris et al. 1989). The NOAEC (no observed adverse effect concentration) for developmental toxicity and maternal toxicity is 300 ml/m³ (Hartwig 2015).

In a study similar to OECD Test Guideline 414, food consumption and the body weight of maternal animals during treatment was reduced after inhalation exposure of Sprague Dawley rats to 0 or 500 ml 1,2-epoxypropane/m³ from day 1 or day 7–16 of gestation for 7 hours per day. Foetal growth of the animals examined on day 21 of gestation was less than that of the control group. No treatment-related malformations arose, only the incidence of wavy ribs (variation) was increased in the treated groups. Food consumption and the body weight of maternal animals was reduced in female New Zealand rabbits after inhalation exposure to 0 or 500 ml 1,2-epoxypropane/m³ from day 1 or day 7–19 of gestation. The foetuses examined on day 30 of gestation showed no developmental toxic effects (Hardin et al. 1983).

Evaluation of a pregnancy risk group for the BAT value

After exposure to 500 ml 1,2-epoxypropane/m³, skeletal variations such as length variants in the seventh cervical rib and wavy ribs in rats as well as no developmental toxic effects with simultaneous maternal toxicity in rabbits were observed. Malformations did not occur. The NOAEC for prenatal developmental toxicity is 300 ml/m³ for rats and 500 ml/m³ for rabbits. Since the 150- or 250-fold margin between the NOAEC and the MAK value of 2 ml/m³ is sufficiently large, 1,2-epoxypropane was assigned to Pregnancy Risk Group C (Hartwig 2015). This also applies taking into account the increased respiratory volume at the workplace.

As 1,2-epoxypropane is assigned to Pregnancy Risk Group C and the BAT value for 1,2-epoxypropane was derived in correlation to the MAK value,

**prenatal effects are not to be expected,
if the BAT value of 2500 pmol N-(2-hydroxypropyl)valine/g globin
in the erythrocyte fraction of whole blood 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.

References

- Bader M (2021) 1,2-Epoxypropane – Addendum for evaluation of a BAT value. Assessment Values in Biological Material – Translation of the German version from 2015. MAK Collect Occup Health Saf: Doc913. https://doi.org/10.34865/bb7556pobeoj21_1ad
- DFG (Deutsche Forschungsgemeinschaft), editor (2019) List of MAK and BAT Values 2019. Maximum Concentrations and Biological Tolerance Values at the Workplace. Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, report 55. Weinheim: Wiley-VCH. <https://doi.org/10.1002/9783527826889>
- Hardin BD, Niemeier RW, Sikov MR, Hackett PL (1983) Reproductive-toxicologic assessment of the epoxides ethylene oxide, propylene oxide, butylene oxide, and styrene oxide. Scand J Work Environ Health 9(2 Spec No): 94–102. <https://doi.org/10.5271/sjweh.2417>
- Harris SB, Schardein JL, Ulrich CE, Ridlon SA (1989) Inhalation developmental toxicity study of propylene oxide in Fischer 344 rats. Fundam Appl Toxicol 13(2): 323–331. [https://doi.org/10.1016/0272-0590\(89\)90268-6](https://doi.org/10.1016/0272-0590(89)90268-6)
- Hartwig A, editor (2015) 1,2-Epoxypropane. MAK Value Documentation, 2013. In: The MAK-Collection for Occupational Health and Safety. Part I: MAK Value Documentations. Weinheim: Wiley-VCH. <https://doi.org/10.1002/3527600418.mb7556e5415>
- Hayes WC, Kirk HD, Gushow TS, Young JT (1988) Effect of inhaled propylene oxide on reproductive parameters in Fischer 344 rats. Fundam Appl Toxicol 10(1): 82–88. [https://doi.org/10.1016/0272-0590\(88\)90253-9](https://doi.org/10.1016/0272-0590(88)90253-9)