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Tetraethyllead

MAK Value Documentation, supplement – Translation of the German version from 2009

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MAK value (1994)	**0.05 mg/m³ (as Pb)**
Peak limitation (2001)	**Category II, excursion factor 2**
Absorption through the skin (1966)	**H**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2008)	**Pregnancy Risk Group B**
Germ cell mutagenicity	**–**
BAT value (1994)	**25 µg diethyllead/l urine (as Pb), 50 µg total lead/l urine**
CAS number	78-00-2

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Developmental toxicity

Prenatal toxicity

The available studies of prenatal developmental toxicity are described in the supplement from 1994 (Greim 2001). The studies relevant for the assessment are summarized in Table 1.

Tab. 1 Studies relevant for the assessment of the developmental toxicity of tetraethyllead

Species, strain, number of animals per group	Exposure	Findings	References
rat, COBS, 20 ♀	**GD 6–16**, 0, 0.1, 1, 10 mg/kg body weight and day, oral, examination on GD 20	**0.1 mg/kg body weight**: dams, foetuses: NOAEL **1.0 mg/kg body weight**: dams: body weight gains ↓; foetuses: resorptions ↑, number of live foetuses ↓ **10 mg/kg body weight**: dams: only 25% pregnant, hypoactivity, tremor, convulsions; foetuses: delayed skeletal development	Kennedy et al. 1975
rat, SD, 3–7 ♀	**GD 9–11** or **GD 12–14**, 0, 7.5, 15, 30 mg/kg body weight and day, oral, examination on GD 22	**7.5 mg/kg body weight and above**: dams: toxic; foetuses: foetal weights ↓ **15 mg/kg body weight**: foetuses: resorptions ↑ (GD 9–11) **30 mg/kg body weight**: dams: lethal	McClain and Becker 1972
mouse, CD1, 20 ♀	**GD 5–15**, 0, 0.01, 0.1, 1, 10 mg/kg body weight and day, oral, examination on GD 18	**0.1 mg/kg body weight**: dams, foetuses: NOAEL **1.0 mg/kg body weight**: dams: body weight gains ↓; foetuses: resorptions ↑, number of live foetuses ↓, delayed skeletal development **10 mg/kg body weight**: dams: only 25% pregnant, hypoactivity, tremor, convulsions	Kennedy et al. 1975

GD: gestation day; NOAEL: no observed adverse effect level; SD: Sprague Dawley

In rats and mice, tetraethyllead doses of 1 mg/kg body weight and day and above led to reduced maternal body weight gains and increased resorptions as well as to a reduced number of live foetuses. The incidence of malformations was not increased. The NOAEL (no observed adverse effect level) for prenatal toxicity for both species is 0.1 mg/kg body weight and day, corresponding to 0.064 mg Pb/kg body weight and day. Lead acetate, for which a NOAEL of 71.4 mg/kg body weight and day (39 mg Pb/kg body weight and day) was obtained, is about 1000 times less toxic than tetraethyllead (Kennedy et al. 1975).

The NOAEL for tetraethyllead of 0.1 mg/kg body weight and day, corresponding to 0.064 mg Pb/kg body weight and day, corresponds to 0.4 mg Pb/m^3 for a person (70 kg body weight; inhaled air volume of 10 m^3 in 8 hours). The margin between this NAEC and the MAK value for tetraethyllead of 0.05 mg/m^3 (calculated as Pb) would thus be sufficiently large to justify Pregnancy Risk Group C for the prenatal toxic effects investigated. Due to the neurotoxic effects of tetraethyllead (see Greim 2001), however, particular consideration must be given to the effects of prenatal exposure on postnatal development.

Postnatal effects after prenatal exposure

There are no studies available for the effects of prenatal exposure to tetraethyllead on the development of the central nervous system (CNS).

In the case of lead and its inorganic compounds, it has been shown that, in humans, damage to the developing nervous system is the most sensitive end point after prenatal exposure. Lead and its inorganic compounds were therefore classified in Pregnancy Risk Group B before withdrawal of the MAK value of 0.1 mg/m^3 in 2004. However,

a direct quantitative comparison with inorganic lead with regard to developmental neurotoxicity is not possible, as organic lead compounds have stronger neurotoxic effects than inorganic lead. Furthermore, the metabolism of organic lead compounds is different from that of inorganic lead compounds. Thus, after exposure to tetraethyllead, not only deethylation and the excretion of triethyllead and especially diethyllead in urine occurs, but also further metabolism to inorganic lead. Diethyllead and total lead in urine are used as parameters for biomonitoring. After exposure to inorganic lead, 95% of the lead is bound to erythrocyte membranes. Therefore, the parameter for the biomonitoring of inorganic lead compounds is lead in whole blood.

A study in neonatal rats given subcutaneous injections of triethyllead, the neurotoxic metabolite of tetraethyllead, in doses of 0, 4.5 or 9 mg/kg body weight (about 0, 2.8, 5.6 mg Pb/kg body weight) on postnatal day 5 confirms that neonatal exposure to organic lead compounds causes CNS damage with hyperreactivity and damage to the hippocampus in adult animals (Booze and Mactutus 1990). A NOAEL was not obtained.

Manifesto (MAK value/classification)

At the MAK value for tetraethyllead of 0.05 mg Pb/m^3, about 200 µg Pb is absorbed in 8 hours (10 m^3; 40% retained). In the studies on which the previous MAK value for inorganic lead of 0.1 mg/m^3 was based, about 300 µg Pb was absorbed in 8 hours (10 m^3; 30% retained). Inorganic lead compounds were assigned to Pregnancy Risk Group B, since adverse effects in exposed children were still detectable at an internal exposure corresponding to 0.1 mg/m^3. As organic lead compounds have stronger neurotoxic effects than inorganic lead compounds and are metabolized also to inorganic lead, it is to be expected that even if the MAK value for tetraethyllead is observed, developmental neurotoxicity will occur as in the case of inorganic lead. Tetraethyllead is therefore assigned to Pregnancy Risk Group B.

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.

References

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