The MAK Collection for Occupational Health and Safety

Addendum to Tetrachloroethylene

Assessment Values in Biological Material – Translation of the German version from 2018

H.M. Bolt[1], H. Drexler[2,*], A. Hartwig[3,*], MAK Commission[4,*]

1 *Leibniz Research Centre for Working Environment and Human Factors, TU Dortmund, Ardeystraße 67, 44139 Dortmund, Germany*

2 *Head of the working group "Assessment Values in Biological Material" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Friedrich-Alexander-Universität Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social, and Environmental Medicine, Henkestraße 9–11, 91054 Erlangen, Germany*

3 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

4 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: H. Drexler (hans.drexler@fau.de), A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

Keywords: tetrachloroethene; 1,1,2,2-tetrachloroethene; tetrachloroethylene; biological tolerance value; BAT value; exposure equivalents for carcinogenic substances; EKA

Citation Note: Bolt HM, Drexler H, Hartwig A, MAK Commission. Addendum to Tetrachloroethylene. Assessment Values in Biological Material – Translation of the German version from 2018. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2019 Oct;4(4):2312–2317]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2025. https://doi.org/10.34865/bb12718e2319_w

Republished (online): 30 Apr 2025

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.bb12718e2319

Addendum completed: 18 Jan 2017

Published (online): 13 Nov 2019

The commission established rules and measures to avoid conflicts of interest.

2312

Addendum to Tetrachloroethylene

BAT value documentation

H.M. Bolt[1], H. Drexler[2,*], A. Hartwig[3,*], MAK Commission[4,*]

DOI: 10.1002/3527600418.bb12718e2319

Abstract

In 2017, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated tetrachloroethylene [127-18-4], considering tetrachloroethylene in blood to characterize the internal exposure at the workplace. Available publications are described in detail.
The exposure equivalents for carcinogenic substances (EKA) of inhaled tetrachloroethylene and tetrachloroethylene in blood were confirmed and extended by recent data. The evaluation of the BAT value was based on the relationship between tetrachloroethylene uptake by inhalation at the MAK value and the corresponding concentration of tetrachloroethylene in blood. An eight-hour exposure at the present MAK value of 10 ml tetrachloroethylene/m^3 correlates, 16 hours after exposure, with a mean tetrachloroethylene concentration in blood of approximately 200 µg/l. Hence, a BAT value of 200 µg tetrachloroethylene/l blood was evaluated. Sampling time is 16 hours after exposure.

Keywords

tetrachloroethylene; perchloroethylene; occupational exposure; biological tolerance value; BAT value; BLW; toxicity

Author Information

[1] Leibniz Research Center for Working Environment and Human Factors, TU Dortmund, Ardeystraße 67, 44139 Dortmund, Germany
[2] Chair of the Working Group "Setting of Threshold Limit Values in Biological Material", Deutsche Forschungsgemeinschaft, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Henkestr. 9–11, 91054 Erlangen, Germany
[3] Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany
[4] Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

* Email: H. Drexler (hans.drexler@fau.de), A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

Addendum to Tetrachloroethylene

BAT (2017)

200 µg tetrachloroethylene/L blood

Sampling time: 16 hours after the end of exposure

EKA (2017)

Correlation between external and internal exposure:

Air Tetrachloroethylene		Blood Tetrachloroethylene
[mL/m³]	[mg/m³]	[µg/L]
3	21	60
10	69	200
20	138	400
30	206	600
50	344	1000

Sampling time: 16 hours after the end of exposure

MAK value (2016)

10 mL/m³ (ppm) ≙ 69 mg/m³

Absorption through the skin (1997)

H

Carcinogenicity (1988)

Category 3B

10 Re-evaluation

Due to limited evidence of a carcinogenic effect (see Guyton et al. 2014), the then valid BAT value for tetrachloroethylene of 1 mg/L blood (at the then valid MAK value of 50 mL/m3) was suspended in 1997 and the substance was classified as a category 3B carcinogen. Instead of the BAT value, an EKA correlation was established (exposure range between 10 and 50 mL/m³, see Schaller and Bolt 2001). The measurement parameter was the tetrachloroethylene concentration in whole blood with sampling being performed 16 hours after the end of shift (beginning of the next shift). This sampling time helps avoid problems caused by the rapid initial wash-out phase after the end of exposure (see Section 10.3). Meanwhile, the MAK value for tetrachloroethylene has been set at 10 mL/m³, which makes it possible to derive a corresponding BAT value (Hartwig 2017).

10.1 Toxicokinetics

Studies have been published in the U.S. to improve the modelling of the toxicokinetics of tetrachloroethylene. These activities, however, did not primarily focus on biomonitoring but rather on species comparison and risk assessment based on data from animal studies using Bayesian statistical methods (Chiu and Ginsberg 2011; Clewell et al. 2005; Covington et al. 2007; Qiu et al. 2010).

These models confirm the low metabolic rate of tetracholoroethylene, with 95th percentile values of 2.1–5.2% (Covington et al. 2007) being reported. For an environmental concentration range of 1 ppb, a metabolic rate of 1.89% (Qiu et al. 2010) was reported. There are major interindividual differences in the extent of metabolism (Chiu et al. 2007; Clewell et al. 2005).

With regard to the biomonitoring of tetrachloroethylene metabolites, the individual significance is severely limited by this considerable interindividual variability. For the main metabolite trichloroacetic acid, its well-known long half-life (approx. 100 hours) poses the problem that results of short-term experimental laboratory exposure can hardly be compared with field data of individuals who have been subjected to long-term occupational exposure (Loizou 2001). Furthermore, trichloroacetic acid is also the main metabolite of the chlorinated hydrocarbons 1,1,2-trichloroethane and 1,1,1-trichloroethane. This speaks for the use of tetrachloroethylene in biological material as a biomonitoring parameter.

10.2 New biomonitoring studies

Against the background of the successful measures to reduce occupational exposure over the past two decades, occupational medical field studies on tetrachloroethylene biomonitoring are available which also include individuals subjected to low levels of exposure (< 10 ppm). These studies focus on dry cleaning staff.

In the study by Gobba et al. (2003), a total of 26 dry cleaning workers in Modena/Italy (16 men, 10 women) were examined, with personal monitoring being performed in the breathing zone using passive samplers for the duration of a shift, blood sampling directly at the end of the shift and urine sampling in the second half of the shift. The day of the week within a working week was not mentioned. The relationships between external exposure and tetrachloroethylene concentrations in blood and urine at the end of the shift were investigated. There is a linear relationship between external exposure and blood concentration even at low exposure levels. For the urinary tetrachloroethylene concentration, a linear relationship is less obvious at low concentrations. The choice of sampling times does not allow a direct comparison with the blood concentrations evaluated by the Commission (sampling 16 hours after the end of exposure).

Maccà et al. (2012) examined 29 men and 42 women working in dry cleaning facilities in the province of Padua/Italy on Thursday and Friday of a working week. The tetrachloroethylene concentration in air was determined using passive samplers. A frequent occurrence of peak concentrations was characteristic. Urine samples were collected before and after each shift, while blood samples were collected on Thursday after the shift and on Friday before the shift. For the pre-shift concentration of tetrachloroethylene in blood (y; mg/L), the formula

$$\mathbf{y = 0.14517 + 0.00303 \cdot (mg/m^3\ tetrachloroethylene)}$$

was used. For the MAK value of 10 mL/m³, this yields a pre-shift value of 0.35 mg tetrachloroethylene/L blood. The pre-shift blood concentrations were thus on the whole higher, compared with the correlation stated by the Commission. No applicable correlation was found between the pre-shift blood and urine concentrations.

In the study by McKernan et al. (2008), 18 women working in dry cleaning facilities in southwest Ohio/U.S. were examined. On three consecutive days (Wednesday to Friday of the working week), the personal exposure to tetrachloroethylene was determined using active samplers. Urine samples were collected before and after each shift; a blood sample was collected on the second day before work commenced. Tetrachloroethylene concentrations in the total group averaged 3.15 mL/m³ on the first two days. The mean blood concentration at the beginning of the shift on the second day was 70.5 µg/L blood. This value is perfectly in line with the linear EKA correlation evaluated by the Commission and proves that this correlation can also be extrapolated to ranges < 10 mL/m³.

10.3 Evaluation of the EKA correlation

Toxicokinetic models confirm that only a very small proportion of incorporated tetrachloroethylene is metabolised, and that there is a great individual variability in metabolism. Therefore, the determination of the main metabolite trichloroacetic acid is not suitable for biomonitoring.

With regard to the determination of tetrachloroethylene in blood, there are significant differences between studies if sampling is performed immediately after the end of the shift. This may be due to the fact that the exact blood sampling time is very important in the initial post-exposure wash-out phase.

The previously evaluated correlation between the tetrachloroethylene concentrations in air and in blood at the beginning of the shift after previous shifts is confirmed by the study conducted by McKernan et al. (2008). According to this study, this correlation is also valid in a low extrapolation range < 10 mL/m³. The higher values measured by Maccà et al. (2012) can possibly be attributed to the frequent occurrence of concentration peaks in the local collective.

This yields the following correlation between external and internal exposure:

Air Tetrachloroethylene		Blood Tetrachloroethylene
[mL/m³]	[mg/m³]	[µg/L]
3	21	60
10	69	200
20	138	400
30	206	600
50	344	1000

Sampling time: 16 hours after the end of exposure

The MAK value of 10 mL tetrachloroethylene/m³ corresponds to a mean concentration (before the next shift) of

200 µg tetrachloroethylene/L blood.

This value has thus been set as the BAT value.

References

Chiu WA, Ginsberg GL (2011) Development and evaluation of a harmonized physiologically based pharmacokinetic (PBPK) model for perchloroethylene toxicokinetics in mice, rats, and humans. Toxicol Appl Pharmacol 253: 203–234

Chiu WA, Micallef S, Monster AC, Bois FY (2007) Toxicokinetics on inhaled trichloroethylene and tetrachloroethylene in humans at 1 ppm: empirical results and comparisons with previous studies. Toxicol Sci 95: 23–36

Clewell HJ, Gentry PR, Kester JE, Anderen ME (2005) Evaluation of physiologically based pharmacokinetic models in risk assessment: an example with perchloroethylene. Crit Rev Toxicol 35: 413–433

Covington TR, Gentry PR, van Landigham CB, Andersen ME, Kester JE, Clewell HJ (2007) The use of Markov chain Monte Carlo uncertainty analysis to support a Public Health Goal for perchloroethylene. Regul Toxicol Pharmacol 47: 1–18

Gobba F, Righi E, Fantuzzi G, Roccatto L, Predieri G, Aggazzotti G (2003) Perchloroethylene in alveolar air, blood, and urine as biologic indices of low-level exposure. J Occup Environ Med 45: 1152–1157

Guyton KZ, Hogan K, Siegel C, Cooper GS, Bale AS, Kopylev L, Barone Jr S, Makris SL, Glenn B, Subramaniam RP, Gwinn MR, Dzubow RC, Chiu WA (2014) Human health effects of tetrachloroethylene: key findings and scientific issues. Environ Health Perspect 122: 325–334

Hartwig A, MAK Commission (2017) Tetrachlorethen [MAK Value Documentation in German language, 2018]. MAK Collect Occup Health Saf 2;
https://doi.org/10.1002/3527600418.mb12718d0063 (last accessed 15.07.2019)

Loizou GD (2001) The application of physiologically based pharmacokinetic modeling in the analysis of occupational exposure to perchloroethylene. Toxicol Lett 124: 59–69

Maccà I, Carrieri M, Scapellato ML, Scopa P, Trevisan A, Bartolucci GB (2012) Biological monitoring of exposure to perchloroethylene in dry cleaning workers. Med Lav 103: 382–393

McKernan LT, Ruder AM, Petersen MR, Hein MJ, Forrester CL, Sanderson WT, Ashley DL, Butler MA (2008) Biological exposure assessment to tetrachloroethylene for workers in the dry cleaning industry. Environ Health 7: 12

Schaller KH, Bolt HM (2001) Addendum zu Tetrachlorethen. In: Lehnert G, Greim H (Eds) Biologische Arbeitsstoff-Toleranz-Werte (BAT-Werte) und Expositionsäquivalente für krebserzeugende Arbeitsstoffe (EKA), 9. Lieferung, Wiley-VCH, Weinheim;
translated (2005): The MAK-Collection for Occupational Health and Safety Part II: BAT Value Documentations, Vol. 5; https://doi.org/10.1002/3527600418.bb12718e0004 (last accessed 03.09.2019)

Qiu J, Chien YC, Bruckner JV, Fisher JW (2010) Baysian analysis of a physiologically based pharmacokinetic model for perchloroethylene in humans. J Toxicol Environ Health A 73: 74–91

Authors: H. M. Bolt, H. Drexler (Chair of the Working Group "Setting of Threshold Limit Values in Biological Material", Deutsche Forschungsgemeinschaft), A. Hartwig (Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft), MAK Commission (Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft)

Approved by the Working Group: 18 January 2017