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Reprint of "Update of the reference and HBM values derived by the German Human Biomonitoring Commission"

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ABSTRACT

In 2007, we reviewed the working principles and working procedures of the German Human Biomonitoring Commission together with the reference values and human biomonitoring (HBM) values derived up to that time. Since then, the Commission has decided to derive additionally HBM I values on the basis of tolerable daily intakes and has used and evaluated this new approach on the metabolites of (2-ethylhexyl) phthalate (DEHP) in urine. Furthermore, the Commission has derived a HBM I value for thallium in urine, has recinded the HBM values for lead in blood, and has updated the HBM values for cadmium in urine. Based on the representative data of the German Environmental Survey on Children from 2003 to 2006 (GerES IV), the Commission has updated the reference values for a large number of environmental pollutants in urine and blood of children in Germany. Since 2007, the Commission has derived new and updated reference values for PFOS and PFOA in human plasma, for thallium in urine, for aromatic amines in urine, for a comprehensive number of phthalate metabolites in urine, and for organochlorine pesticides in human breast milk. Furthermore, the Commission has evaluated background exposure levels for two naphthalene metabolites and acrylamide (using acrylamide-haemoglobin adduct) for the general population. This paper reports the new values, including those already published, in order to provide an updated overview.

Introduction

Human biomonitoring (HBM) is defined as the measurement of concentrations of chemicals or their metabolites in human biological media such as blood, urine or breast milk. It may include chemical and biological parameters which allow inferences about the pollutants' biological effects. HBM is considered the method of choice for determining internal exposures in the population, population groups or individuals, thereby supplying a basis for estimating health risks and, if necessary, for risk management (Angerer et al., 2007). Furthermore, HBM is a prominent feature of the exposure assessment component of environmental epidemiology studies which evaluate potential associations between exposure to chemicals and health effects.

Several concepts have been established for the interpretation of HBM data (Hays et al., 2008; Angerer et al., 2011). In Germany, the Human Biomonitoring Commission was established in 1992. The working principles, the working procedures and basic criteria for defining statistically based reference values and health-related HBM values derived from epidemiological studies were summarized by Ewers et al. (1999) and updated by Schulz et al. (2007). The reference value for a chemical substance in human biological material (e.g., blood, urine) is derived statistically from a series of measurements, ideally obtained from a representative sample of the general population. The HBM Commission uses the 95% confidence interval for the 95 population percentile to derive the reference value. To derive it, it is rounded off within the 95% confidence interval. The reference value thus permits to compare the exposure of individuals or population groups to the exposure of the general population. HBM values are health-related biological exposure limit values. The HBM Commission defines two different types of HBM values: HBM I and HBM II. The HBM II value represents the concentration above which there is an increased risk for adverse health effects. The HBM II value should thus be regarded as an intervention or "action level". The HBM I value corresponds to the concentration of a substance in human biological material below which no adverse health effects are expected. The HBM I value should thus be regarded as verification or "control value". In the case of a concentration of a substance in the range between

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Table 1
Reference values (RV_{95}) for antimony, arsenic, cadmium, lead, mercury, nickel, thallium, platinum, uranium in urine or blood (sources in brackets).

Parameter and matrix (reference)	Population group (age range)	Study period	RV_{95}[a]
Antimony in urine (Schulz et al., 2009)	Children (3–14 years)	2003–2006	0.3 µg/l
Arsenic in urine (Wilhelm et al., 2004; Schulz et al., 2009)	Children who did not eat fish 48 h prior to sample collection (3–14 years)	2003–2006	15.0 µg/l
	Adults who did not eat fish 48 h prior to sample collection (18–69 years)	1997–1999	
Cadmium in urine (Wilhelm et al., 2004; Schulz et al., 2009)	Non-smoking children (3–14 years)	2003–2006	0.2 µg/l
	Non-smoking adults (18–69 years)	1997–1999	0.8 µg/l
Cadmium in blood (Wilhelm et al., 2004; Schulz et al., 2009)	Non-smoking children (3–14 years)	2003–2006	<0.3 µg/l[b]
	Non-smoking adults (18–69 years)	1997–1999	1.0 µg/l
Lead in blood (Wilhelm et al., 2004; Schulz et al., 2009)	Children (3–14 years)	2003–2006	35 µg/l
	Women (18–69 years)	1997–1999	70 µg/l
	Men (18–69 years)	1997–1999	90 µg/l
Mercury in urine (Wilhelm et al., 2004; Schulz et al., 2007)	Children without dental amalgam fillings (3–14 years)	2003–2006	0.4 µg/l
	Adults without dental amalgam fillings (18–69 years)	1997–1999	1.0 µg/l
Mercury in blood (Wilhelm et al., 2004; Schulz et al., 2009)	Children who ate fish ≤ 3 times per month (3–14 years)	2003–2006	0.8 µg/l
	Adults who ate fish ≤ 3 times per month (18–69 years)	1997–1999	2.0 µg/l
Nickel in urine (Wilhelm et al., 2004; Schulz et al., 2009)	Children (3–14 years)	2003–2006	4.5 µg/l
	Adults (not a strictly representative sample)	Not specified	3 µg/l
Platinum in urine (Wilhelm et al., 2004)	Adults without dental inlays, crowns or bridge elements made of precious metal (18–69 years)	1997–1999	0.01 µg/l
Thallium in urine (Schulz et al., 2009; HBM Commission, 2011a)	Children (3–14 years)	2003–2006	0.6 µg/l
	Adults (20–29 years)[c]	2000–2008	0.5 µg/l
Uranium in urine (HBM Commission, 2005; Schulz et al., 2009)	Children (3–14 years)	2003–2006	0.04 µg/l
	Adults (not a strictly representative sample)	2001–2003	0.03–0.06 µg/l[d]

[a] Uncertainty of analysis must be taken into account.
[b] NO reference value, but should there be analytically reliable and confirmed concentrations of Cd in whole blood above the level of 0.3 µg/l, a special exposure must be expected such as active smoking, i.e.
[c] Data obtained from the German Environmental Specimen Bank (ESB) for human tissues.
[d] This background exposure level should be used for orientation purposes unless data are available from a representative population sample.

HBM I and HBM II value health effects cannot be excluded with sufficient certainty.

A summary of reference and HBM values which have been set by the Commission until 2007 is available in Schulz et al. (2007).

This paper gives an update of the recommendations by the Human Biomonitoring Commission since then. These include revised reference and HBM values, new reference and HBM values, recommendations in case reference values are exceeded, a new tox-icological approach to derive HBM values, and a critical evaluation of some values which were not revised. For the sake of completeness, all reference and HBM values set until June 2011 have been summarised in Tables 1–13.

Reference values (RV_{95})

The reference value (RV_{95}) of the HBM Commission is based on the 95% confidence interval of the 95th population percentile of the concentration level of the respective parameter in the matrix obtained from the reference population. The reference value is derived by rounding off the 95th population percentile within the

Table 2
Reference values (RV_{95}) for chlorophenols in urine of children and adults (HBM Commission, 2009c; Schulz and Butte, 2007) and pentachlorophenol in serum of adults (HBM Commission, 1999a,b).

Parameter	Population group (age range)	Study period	RV_{95}[a]
2-Monochlorophenol	Children (3–14 years)	2003–2006	7.0 µg/**l**
4-Monochlorophenol	Children (3–14 years)	2003–2006	15 µg/l
	Adults (18–69 years)	1997–1999	
2,4-Dichlorophenol	Children (3–14 years)	2003–2006	2 µg/l
	Adults (18–69 years)	1997–1999	3 µg/l
2,5-Dichlorophenol	Children (3–14 years)	2003–2006	6 µg/l
	Adults (18–69 years)	1997–1999	20 µg/l
2,6-Dichlorophenol	Children (3–14 years)	2003–2006	<0.3 µg/l[b]
	Adults (18–69 years)	1997–1999	
2,3,4-Trichlorophenol	Children (3–14 years)	2003–2006	<0.3 µg/l[b]
	Adults (18–69 years)	1997–1999	
2,4,5-Trichlorophenol	Children (3–14 years)	2003–2006	0.5 µg/l
	Adults (18–69 years)	1997–1999	1 µg/l
2,4,6-Trichlorophenol	Children (3–14 years)	2003–2006	0.7 µg/l
	Adults (18–69 years)	1997–1999	1.5 µg/l
2,3,4,6-Tetrachlorophenol	Children (3–14 years)	2003–2006	<0.3 µg/l[b]
	Adults (18–69 years)	1997–1999	1.0 µg/l
Pentachlorophenol (PCP) in urine	Children (3–14 years)	2003–2006	2.0 µg/l[b]
	Adults (18–69 years) living in homes without wood preservatives	1997–1999	5 µg/l
PCP in serum	Adults (not a strictly representative sample)	1995–1996	12 µg/l

[a] Uncertainty of analysis must be taken into account.
[b] No reference value, but should there be analytically reliable and confirmed concentrations above the mentioned value a special exposure must be expected.