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HBM4EU WP10: Input to consultation on OEL report ECHA

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In HBM4EU aggregated data were obtained in a standardized and comparable way from existing European data collections for 1st and 2nd set prioritized substances. One of these substance groups was cadmium. Based on these data, we collected information on the human exposure levels in Europe. From these aggregated data, we extracted the obtained data for cadmium from European studies with samples collected between 2005 and 2015. Aggregated data for cadmium concentration in urine, blood or breast milk samples were reported in 4 studies involving newborns, 15 studies involving children, in 9 studies involving teenagers and in 30 studies involving adults (see attached Excel HBM4EU WP10_Overview_Cadmium data). All studies included at least 60 participants and samples were collected between 2005 and 2015.

The reported median-values and 95th percentiles of the individual studies in the table below were averaged (by taking the median) over the different studies of newborns, children, teenagers and adults. Median urinary and blood cadmium levels are higher in adults compared to children and teenagers. Health-based reference values for cadmium in urine are 1 µg/L (µg/g creatinine; HBM I) and 4 µg/L (µg/g creatinine; HBM II) for adults, and 0.5 µg/L (µg/g creatinine; HBM I) and 2 µg/L (µg/g creatinine; HBM II) for children, as set by the German Human Biomonitoring Commission [1]. In blood, reference value is below 1 µg/L for adults [2] . In addition, reference values (RV_{95}) for cadmium in urine is 0.2 µg/l for non-smoking children (3-14 years) and 0.8 µg/l for non-smoking adults (18-69 years) [1]. RV_{95} is defined by the German HBM Commission as the 95th percentile of measured concentrations of a substance in the relevant matrix of a reference population. Canadian RV_{95} for cadmium are also available; 0.69 µg/l for children between 3-5 years, 0.68 µg/l for children and teenagers between 6 and 19 years and 1.3 µg/l for adults between 20- 79 years old [3]. The aggregated data for urinary cadmium concentrations reported in the table below, are well within the range of the German and Canadian reference values.

The individual data collections prepared and made available within HBM4EU also contained aggregated data stratified by sex and educational level (see attached Excel HBM4EU WP10_Overview_Cadmium data). From these stratifications a trend can be seen that urinary cadmium concentrations adjusted for creatinine are generally higher in female adults than males. This is also observed in literature and is explained by an increased gastrointestinal absorption of cadmium due to lower iron levels in females [4, 5]. But no associations between cadmium and gender in children and teenagers were observed. There seems a trend that adults with a higher educational level have lower urinary cadmium exposure levels compared with adults with a low to medium educational level. A prudent assumption to explain this observation is that participants with a lower educational level may smoke and smoking was associated with higher cadmium levels in urine and blood [5].

Source data: merged harmonized aggregated data obtained from Deliverable D10.6 (2nd annual list of exposure distributions and/or European reference values) (version dated 26/12/2019), Excluded data collections before 2005 and after 2015.

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Table: Summary statistics describing urinary concentrations of cadmium (µg/L & µg/g crt) in the European population stratified for children (3-11 years), teenagers (12-19y), and adults (≥20y) based on studies included in the HBM4EU harmonized aggregated data (sampling years between 2005-2015)

Cadmium in urine				
		Children 3-11y	Teenagers 12-19y	Adults ≥20y
Median	µg/L	0.13	0.28	0.24
	µg/g crt	0.12	0.20	0.21
P95	µg/L	0.30	0.67	0.71
	µg/g crt	0.24	0.41	0.57
Number of studies*		13	4	21

*N in each individual study is at least 60

Table: Summary statistics describing (cord) blood concentrations of cadmium (µg/L) in the European population stratified for newborns (0y), children (3-11 years), teenagers (12-19y), and adults (≥20y) based on studies included in the HBM4EU harmonized aggregated data (sampling years between 2005-2015)

Cadmium in blood					
		Newborns 0y	Children 3-11y	Teenagers 12-19y	Adults ≥20y
Median	µg/L	0.04	/	0.18	0.40
P95	µg/L	0.07	/	0.54	1.93
Number of studies*		4	2	5	7

*N in each individual study is at least 60

Reference list

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2. Wilhelm, M., U. Ewers, and C. Schulz, *Revised and new reference values for some trace elements in blood and urine for human biomonitoring in environmental medicine.* International Journal of Hygiene and Environmental Health, 2004. **207**(1): p. 69-73.
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4. Vacchi-Suzzi, C., et al., *Is Urinary Cadmium a Biomarker of Long-term Exposure in Humans? A Review.* Curr Environ Health Rep, 2016. **3**(4): p. 450-458.
5. Adams, S.V. and P.A. Newcomb, *Cadmium blood and urine concentrations as measures of exposure: NHANES 1999-2010.* J Expo Sci Environ Epidemiol, 2014. **24**(2): p. 163-70.