The MAK-Collection for Occupational Health and Safety

GMS PUBLISSO ZB MED-Publikationsportal Lebenswissenschaften

Aluminium – Addendum for evaluation of a BAR

Assessment Values in Biological Material – Translation of the German version from 2019

K. Klotz[1]
H. Drexler[2,*]
A. Hartwig[3,*]
MAK Commission[4,*]

1 *Employer's liability insurance association for wood and metal, Weinmarkt 9–11, 90403 Nürnberg, Germany*
2 *Chair of the Working Group "Setting of Threshold Limit Values in Biological Materials", 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*

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

Keywords

aluminium, BAR, biological reference value

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated a biological reference value (BAR) for aluminium [7429-90-5] in 2018. Available publications are summarised.

Considering the available studies analysing aluminium in urine, a BAR of 15 µg aluminium/g creatinine was established. Sampling time is for long-term exposures at the end of the shift after several shifts. For aluminium in blood, the data base it not sufficient for the evaluation of a BAR.

Citation Note:
Klotz K, Drexler H, Hartwig A, MAK Commission. Aluminium – Addendum for evaluation of a BAR. Assessment Values in Biological Material – Translation of the German version from 2019. MAK Collect Occup Health Saf. 2020 May;5(1):Doc014.
DOI: 10.34865/bb742990e5_1

Manuscript completed:
16 Mar 2018

Publication date:
11 May 2020

BAR (2018)	**15 µg aluminium/g creatinine** Sampling time: for long-term exposures: at the end of the shift after several shifts
BAT (2017)	**50 µg aluminium/g creatinine** Sampling time: for long-term exposures: at the end of the shift after several shifts
MAK value	**1.5 mg/m³ R (1997)** **4 mg/m³ I (2006)**
Absorption through the skin	–
Carcinogenicity	–

Re-evaluation

In 2017, a BAT value for aluminium of 50 µg/g creatinine was established, which is based on effects described in the addendum of 2018 (translated 2019, Klotz et al. 2019). As critical end point neurotoxicity was taken into account. In this addendum, it is examined if the derivation of a biological reference value (BAR) is possible. Due to the wide-ranging debate about the risks of exposure to aluminium of the general population as well as after occupational exposure it appears useful to the Commission, in addition to the BAT value, to evaluate a biological reference value which is oriented towards the background exposure of the general population.

Background exposure

An overview of the available studies in which the aluminium concentrations were analysed in the urine or in the plasma of persons without occupational exposure to aluminium is shown in Table 1.

Tab. 1 Studies on the levels of aluminium in the urine and blood of persons without occupational exposure to aluminium

References	Country	Collective (age)	Aluminium		Remarks
			in urine	in blood	
Hoet et al. 2013	Belgium	460 ♂, 541 ♀ (40.1 ± 12.3; 18–80 years)	median: 2.2 µg/l P95: 9.3 µg/l median: 2.0 µg/g crea P95: 7.5 µg/g crea		Spot urine, non-fasted, ICP-MS; LOD: 1.57 µg/l
Morton et al. 2014	Great Britain	132 (50 ♀, 82 ♂) Al-workers of the HSL without exposure (no data)	median: 3.8 µg/l P95: 25.7 µg/l		ICP-MS; LOQ: 1.3 µg/l
Sieniawska et al. 2012	Great Britain	111 healthy adults, 77 ♂, 34 ♀, 24-h urine (21–85 years)	median: 5.4 µg/24 h CI 0.95: < LOD–22 µg/24 h median: 3.9 µg/g crea CI 0.95: < LOD–13.9 µg/g crea		ICP-MS; LOD: 0.8 µg/l
Goullé et al. 2005	France	100 healthy volunteers (no data)	median: 1.9 µg/l P95: 11.2 µg/l	median: 1.3 µg/l B P95: 6.4 µg/l B median: 3.1 µg/l P P95: 17.3 µg/l P	ICP-MS; LOQ: 1.1 µg/l U, 8.1 µg/l B, 7.7 µg/l P
Deschamps et al. 2009	France	60 ♂ workers without Al exposure (35.8 ± 8.15 years)	4.4 ± 3.7 µg/l (range 0.2–17.5 µg/l)	3.3 ± 3.4 µg/l P (range 0.1–24.1 µg/l) P	morning urine fasted, ET-AAS; LOD: 2 µg/l
Dereumeaux et al. 2016	France	990 pregnant (18–47 years)			ICP-MS; LOQ: 1 µg/l; no measured values, contamination of the blood value
Nisse et al. 2017	France	1016 ♂, 976 ♀ (20–59 years), previously a highly polluted industrial area	n = 1910 median: 3.1 µg/l P95: 11.5 µg/l ♀ P95: 12.7 µg/l ♂ P95: 9.9 µg/l median: 2.4 µg/g crea P95: 13.3 µg/g crea ♀ P95:14.8 µg/g crea ♂ P95: 10.2 µg/g crea	n = 1992 median: 3.1 µg/l B P95: 11.2 µg/l B ♀ P95: 11.2 µg/l B ♂ P95: 11.3 µg/l B	ICP-MS; LOD: 0.3 µg/l; (blood values analysed in B&D sample tubes and Sarstedt monovettes); levels were lower (median: 0.6 µg/l B, P95 6.7 µg/l B) in that part of the analyses using Sarstedt monovettes (n = 121)

Tab. 1 *(continued)*

References	Country	Collective (age)	Aluminium		Remarks
			in urine	in blood	
Cabral Pinto et al. 2017	Portugal	103 inhabitants of the Portuguese town of Estarreja (> 55 years)	median: 18 µg/g crea mean: 4299 ± 16,500 µg/g crea		ICP-MS; residents of an industrial area with previous high environmental contamination
Minoia et al. 1990	Italy (Lombardy)	no data	n = 766 mean: 10.9 µg/l (range: 1–31 µg/l)	n = 916 mean: 6 ± 0.4 µg/l S (range: 1–10.9 µg/l) S	flame-AAS, ET-AAS, ICP-AES
Alimonti et al. 2005	Italy	110 healthy volunteers from Rome (20–61 years)	no data	median: 2.0 µg/l S P95: 5.3 µg/l S median: 15.3 µg/l B P95: 33.3 µg/l B	ICP-MS
Bonforte et al. 1998	Italy	20 persons (no data)	no data	6 ± 0.4 µg/l P	GF-AAS; LOD: not specified
Forrer et al. 2001	Switzerland	110 volunteers (no data)		median: 10.0 µg/l S P95: 18.7 µg/l S mean: 11.0 ± 9.0 µg/l S	ICP-MS; LOD: 0.03 µg/l
Valkonen und Aitio 1997	Finland	44 persons (no data)	n = 44 mean: 8.9 ± 4.9 µg/l (range 1.9–22.1 µg/l) P95 17.0 µg/l	n = 21 mean: 1.6 ± 0.8 µg/l (range: 0.5–3.5 µg/l) S P95: 2.4 µg/l S	GF-AAS; LOD 0.5 µg/l S, 1.9 µg/l U
Zeiner et al. 2004	Hungary	100 persons of the general population (24–59 years)	median: 9.9 µg/g crea mean: 22.5 ± 45.8 µg/g crea (range < LOD–308.7 µg/g crea)	no data	ICP-MS; LOD: 0.1–0.5 µg/l for all analysed elements
Wilson et al. 2011	South Africa	45 ♂, 62 ♀ volunteers (18–73 years)	n = 94 mean: 23.7 µg/g crea median: 17.7 µg/g crea (range 7.2–66.7 µg/g crea)	n = 92 mean: 8.0 B (range: 0.7–40.9 µg/l B)	ET-AAS; discussed cause for higher Al levels than in other studies: contamination or Al in everyday life
Henríquez-Hernández et al. 2017	Spain	245 Africans who have recently started to live in Spain (no details)	no data	median: 60 µg/l B mean: 144.4 ± 641.3 B (range: 0.4–9323 µg/l)	ICP-MS
Kim et al. 2017	Korea	119 ♂, 139 ♀ (12–78 years)	no data	GM: 10.6 µg/l B P95: 18.6 µg/l B	ICP-MS

Tab. 1 *(continued)*

References	Country	Collective (age)	Aluminium		Remarks
			in urine	in blood	
Wang et al. 1991	Kanada	63 healthy adults (24–62 years)	mean: 6.5 ± 3.5 µg/l P97.5: 13.5 µg/l	mean: 1.6 ± 1.4 µg/l S P97.5: 5 µg/l S	GF-AAS; LOD: 0.8 µg/l S, LOD: 0.5 µg/l U
Komaromy-Hiller et al. 2000	USA	no data	mean: 13.4 ± 11.4 µg/l median: 11.0 µg/l P95 adj: 36.1 µg/l mean: 17.5 ± 15.9 µg/g crea median: 13.2 µg/g crea P95 adj: 49.3 µg/g crea		

Aluminium: 1 µmol/l = 26.98 µg/l crea; µg/g = µg/g creatinine
AAS = atomic absorption spectrometry; adj = adjusted; B = blood; CI = confidence interval; ET = electrothermal; GF = graphite furnace; GM = geometric mean; HSL = Health and Safety Laboratory; ICP-MS = inductively coupled plasma mass spectrometry; LOD = limit of detection; LOQ = limit of quantification; P = plasma; P95 = 95th percentile; P97.5 = 97.5th percentile; S = serum; U = urine

In the assessment of the available data, it has to be taken into account that the analysis of aluminium has to be carried out with particular care. There is a high risk of contamination due to its ubiquitous occurrence. There can be interferences both in the pre-analytical phase (due to the extremely high background exposure) and in the analytical phase (for example spectral interferences in atomic absorption spectroscopy and inductively coupled plasma mass spectrometry).

Contamination in the pre-analytical phase can largely be prevented by the use of suitable urine beakers which are not opened until directly prior to sampling and by dispatching the urine sample in this beaker without refilling.

Evaluation of the biological reference value (BAR)

For the derivation of a biological reference value (BAR) the background exposure of persons of working age occupationally not exposed to aluminium is presented; this value is oriented towards the 95th percentile. At present, there are no data available on the background exposure in Germany. Table 2 shows an overview of the studies listing the 95th percentiles of the aluminium concentration in urine, blood, plasma and serum.

Tab. 2 Studies relevant for the evaluation with indication of the 95th percentile (P95) for the derivation of the BAR

References	n	Urine P95 Al [µg/g crea]	Blood P95 Al [µg/l]	Plasma P95 Al [µg/l]	Serum P95 Al [µg/l]
Hoet et al. 2013[b)]	1022	7.5			
Morton et al. 2014	132	21.4[a)]			
Goullé et al. 2005	100	9.3[a)]	6.4	17.3	
Nisse et al. 2017	1910	13.3	11.2		
Alimonti et al. 2005	110		33.3		5.3
Forrer et al. 2001	110				18.7
Valkonen and Aitio 1997	44	14.2[a)]			2.4
Kim et al. 2017[c)]	258		18.6		

[a)] value calculated from µg/l: 1.2 µg Al/l = 1 µg Al/g creatinine
[b)] age of investigated persons: 18–80 years
[c)] age of investigated persons: 12–78 years

For the determination of aluminium in urine a few studies with a high number of examined persons (up to n = 1910) are available (Table 1). Five of these studies give 95th percentiles for the urinary elimination of aluminium in the range between 7.5 and 21.4 µg/g creatinine. Based on these data a

BAR of 15 µg aluminium/g creatinine

is derived.

For the determination of aluminium concentrations in blood, plasma and serum only a comparatively small number of studies is available and the results for the 95th percentiles scatter in a wide range. Further studies are therefore necessary to evaluate a BAR for aluminium in blood, plasma or serum.

References

Alimonti A, Bocca B, Mannella E, Petrucci F, Zennaro F, Cotichini R, D'Ippolito C, Agresti A, Caimi S, Forte G (2005) Assessment of reference values for selected elements in a healthy urban population. Ann Ist Super Sanita 41: 181–187. http://old.iss.it/publ/anna/2005/2/412181.pdf, accessed 18 Dec 2019

Bonforte G, Surian M, Dozio B, Scanziani R, Baj A, Colombo S, Toffoletto F (1998) Plasma or whole blood concentrations of trace elements in patients treated by haemodiafiltration with on-line prepared substitution fluid. Nephrol dial transplan 13 Suppl 5: 29–33. DOI: 10.1093/ndt/13.suppl_5.29

Cabral Pinto MM, Marinho-Reis AP, Almeida A, Ordens CM, Silva MM, Freitas S, Simoes MR, Moreira PI, Dinis PA, Diniz ML, Ferreira Da Silva EA, Condesso De Melo MT (2017) Human predisposition to cognitive impairment and its relation with environmental exposure to potentially toxic elements. Environ Geochem Health 40: 1767–1784. DOI: 10.1007/s10653-017-9928-3

Dereumeaux C, Saoudi A, Pecheux M, Berat B, De Crouy-Chanel P, Zaros C, Brunel S, Delamaire C, Le Tertre A, Lefranc A, Vandentorren S, Guldner L (2016) Biomarkers of exposure to environmental contaminants in French pregnant women from the Elfe cohort in 2011. Environ Int 97: 56–67. DOI: 10.1016/j.envint.2016.10.013

Deschamps FJ, Lesage FX, Chobriat J, Py N, Novella JL (2009) Exposure risk assessment in an aluminium salvage plant. J Occup Environ Med 51: 1267–1274. DOI: 10.1097/JOM.0b013e3181bc2d35

Forrer R, Gautschi K, Lutz H (2001) Simultaneous measurement of the trace elements Al, As, B, Be, Cd, Co, Cu, Fe, Li, Mn, Mo, Ni, Rb, Se, Sr, and Zn in human serum and their reference ranges by ICP-MS. Biol Trace Elem Res 80: 77–93. DOI: 10.1385/BTER:80:1:77

Goullé JP, Mahieu L, Castermant J, Neveu N, Bonneau L, Laine G, Bouige D, Lacroix C (2005) Metal and metalloid multi-elementary ICP-MS validation in whole blood, plasma, urine and hair. Reference values. Forensic Sci Int 153: 39–44. DOI: 10.1016/j.forsciint.2005.04.020

Henríquez-Hernández LA, Luzardo OP, Boada LD, Carranza C, Perez Arellano JL, Gonzalez-Antuna A, Almeida-Gonzalez M, Barry-Rodriguez C, Zumbado M, Camacho M (2017) Study of the influencing factors of the blood levels of toxic elements in Africans from 16 countries. Environ Pollut 230: 817–828. DOI: 10.1016/j.envpol.2017.07.036

Hoet P, Jacquerye C, Deumer G, Lison D, Haufroid V (2013) Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium. Clin Chem Lab Med 51: 839–849. DOI: 10.1515/cclm-2012-0688

Kim H-J, Lim H-S, Lee K-R, Choi M-H, Kang NM, Lee CH, Oh E-J, Park H-K (2017) Determination of trace metal levels in the general population of Korea. Int J Environ Res Public Health 14: 702. DOI: 10.3390/ijerph14070702

Klotz K, Meyer-Baron M, van Thriel C, Pallapies D, Nasterlack M, Letzel S, Roßbach B, Triebig G, Weistenhöfer W, Drexler H, Hartwig A, MAK Commission (2019) Addendum to aluminium. BAT Value Documentation, 2018. MAK Collect Occup Health Saf 4: 2279–2311. DOI: 10.1002/3527600418.bb742990vere2419

Komaromy-Hiller G, Ash KO, Costa R, Howerton K (2000) Comparison of representative ranges based on U.S. patient population and literature reference intervals for urinary trace elements. Clin Chim Acta 296: 71–90. DOI: 10.1016/S0009-8981(00)00205-9

Minoia C, Sabbioni E, Apostoli P, Pietra R, Pozzoli L, Gallorini M, Nicolaou G, Alessio L, Capodaglio E (1990) Trace-element reference values in tissues from inhabitants of the European Community I. A Study of 46 elements in urine, blood and serum of Italian subjects. Sci Total Environ 95: 89–105. DOI: 10.1016/0048-9697(90)90055-y

Morton J, Tan E, Leese E, Cocker J (2014) Determination of 61 elements in urine samples collected from a non-occupationally exposed UK adult population. Toxicol Lett 231: 179–193. DOI: 10.1016/j.toxlet.2014.08.019

Nisse C, Tagne-Fotso R, Howsam M, Members of Health Examination Centres of the Nord – Pas-de-Calais region network, Richeval C, Labat L, Leroyer A (2017) Blood and urinary levels of metals and metalloids in the general adult population of Northern France: The IMEPOGE study, 2008–2010. Int J Hyg Environ Health 220: 341–363. DOI: 10.1016/j.ijheh.2016.09.020

Sieniawska CE, Jung LC, Olufadi R, Walker V (2012) Twenty-four-hour urinary trace element excretion: reference intervals and interpretive issues. Ann Clin Biochem 49: 341–351. DOI: 10.1258/acb.2011.011179

Straff W, Möller M, Jakobi N, Weishoff-Houben M, Dott W, Wiesmüller GA (2002) Predictive value of human biomonitoring in environmental medicine: Experiences at the outpatient unit of environmental medicine (UEM) of the University Hospital Aachen, Germany. Int J Hyg Environ Health 205: 337–346. DOI: 10.1078/1438-4639-00160

Valkonen S, Aitio A (1997) Analysis of aluminium in serum and urine for the biomonitoring of occupational exposure. Sci Total Environ 199: 103–110. DOI: 10.1016/S0048-9697(97)05485-5

Wang ST, Pizzolato S, Demshar HP (1991) Aluminum levels in normal human serum and urine as determined by Zeeman atomic-absorption spectrometry. J Anal Toxicol 15: 66–70. DOI: 10.1093/jat/15.2.66

Wilson K, Kielkowski D, Theodoru P, Naik I (2011) A trace metal survey of non-occupationally exposed Gauteng residents. Biol Trace Elem Res 143: 66–78. DOI: 10.1007/s12011-010-8846-3

Zeiner M, Ovari M, Zaray G, Steffan I (2004) Reference concentrations of trace elements in urine of the Budapestian population. Biol Trace Elem Res 101: 107–115. DOI: 10.1385/BTER:101:2:107