

Aniline – Addendum: evaluation of a BAR

Assessment Values in Biological Material – Translation of the German version from 2026

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Abstract

The German Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) evaluated the data for aniline [62-53-3] to derive a biological reference value (BAR). The 95th percentiles of background concentrations in the urine of occupationally unexposed persons ranged between 6.5 and 14.5 µg aniline/l. Based on available studies, a weighted mean value of the 95th percentile of 13.3 µg aniline/l can be calculated. Therefore, a BAR of 15 µg aniline (after hydrolysis)/l urine has been derived for aniline. The BAR applies to both smokers and non-smokers, as the urine concentrations did not differ significantly. Sampling should take place at the end of exposure or at the end of the shift.

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BAR (2025)	15 µg aniline (after hydrolysis)/l urine
BAT value (2015)	500 µg aniline (after hydrolysis)/l urine^{a)}
	Sampling time: End of exposure or end of shift
Prenatal toxicity (2024)	Pregnancy Risk Group B, prerequisite for Pregnancy Risk Group C: 30 µg aniline (after hydrolysis)/l urine
BLW (2015)	100 µg aniline (released from haemoglobin conjugate)/l blood
	Sampling time: after exposure for at least 3 months
MAK value (1983)	2 ml/m³ $\approx$ 7.7 mg/m³
Absorption through the skin (1981)	H
Carcinogenicity (2004)	Category 4

^{a)} BAT value derived as the maximum value due to acute toxic effects (formation of methaemoglobin)

In 2015, a BAT value of 500 µg aniline (after hydrolysis)/l urine was derived for aniline from the study data by Kafferlein et al. (2014) as the maximum value due to acute toxic effects. The formation of methaemoglobin was the critical endpoint (translated in Bolt et al. 2017). The BAT value was confirmed in 2024 and the substance was designated into Pregnancy Risk Group B with a note regarding prerequisites for Pregnancy Risk Group C at a concentration of 30 µg aniline/l urine (Brinkmann et al. 2025).

Metabolism and toxicokinetics

Data on metabolism and toxicokinetics in both humans and animals have been comprehensively described in Hartwig (translated in 2010), Hartwig and MAK Commission (translated in 2019), Bolt et al. (2017), and Brinkmann et al. (2025).

Critical toxicity

The formation of methaemoglobin is considered the critical effect of aniline in humans, whereby an increase in methaemoglobin content to a value over 1.5% indicates exposure to methaemoglobin-forming agents. Hazardous health effects from methaemoglobin are not expected in healthy adults at methaemoglobin concentrations up to 5% (translated in Leng et al. 2016).

Background exposure

The following exposure sources have been listed as contributors to background aniline levels (HBM-Kommission 2011; see Table 1): tobacco smoke, pharmaceuticals, pesticide residues, pigments and stabilisers in cosmetics, oxidising hair dyes, food colourants, black tea, aquatic environment, leather products, rubber products, tyres. The daily intake of aniline from fruit and vegetables is reported to be 0.11 mg/kg body weight (EU 2004); this value would correspond with a workplace-air exposure level of about 0.8 mg aniline/m³ (0.2 ml/m³; 70 kg body weight; 10 m³ respiratory volume).

Tab. 1 Sources of background exposure to aniline (per HBM-Kommission 2011)

Sources	Examples (substances/occurrences)
Tobacco smoke	
Pharmaceuticals	Novalgin, phenylbutazone
Pesticide residues	Carboxin, chloridazone, carbetamide, propham, desmedipham, pencycuron
Pigments in cosmetics	Pigment Red 64:1, Acid Orange 10, Acid Red 1 and 33, Disperse Yellow 16, Acid Yellow 11,
Stabilisers in cosmetics	Solvent Red 23 and 73, Acid Black 1, Disperse Violet 23/27, Basic Blue 26, acetanilide, N-phenyl-p-
Oxidising hair dyes	phenylenediamine and salts
Refills for ink and ballpoint pens	
Food colourants	Red 2G
Black tea	
Aquatic environment	Surface waters, landfill leachate, sites contaminated by armament disposal
Leather products	
Rubber products/tyres	Diphenylguanidine as a vulcanisation accelerator

To derive a reference value, the HBM Commission cited a collective of 856 non-smokers (age > 18 years) from a study by Kütting et al. (2009). Urinary concentrations with a median value of 2.99 µg aniline/l urine and a 95th percentile of 14.49 µg aniline/l urine (range < 0.05–384 µg aniline/l urine) were ascertained (HBM-Kommission 2011; Kütting et al. 2009).

In another study on 81 non-smokers (48 women, 33 men; aged 20–61 years) from the general population, the median was reported as 1.88 µg aniline/l urine, the 95th percentile as 10.9 µg aniline/l urine and the range as 0.5–130 µg aniline/l urine (Seidel 2005).

Weiß (2005) investigated urine samples from 100 individuals from the general population (no data on sex) from the Ruhr region in Germany (median age of 38.5 years, range: 22–73 years; median weight of 73 kg) as well as 100 individuals from the Münsterland area of Germany (median age of 40 years, range: 20–68 years; median weight of 71 kg). For the collective of non-smokers (n = 115), a 95th percentile of 8.2 µg aniline/l urine was determined, whereas values of 6.5 µg aniline/l urine and 7.5 µg aniline/l urine were found for secondhand smokers (n = 37) and smokers (n = 45), respectively.

Additional studies on background aniline exposure in urine are presented in Table 2 (modified according to HBM-Kommission 2011).

Tab. 2 Studies on background exposure to aniline in urine [µg/l] in the general population (see also HBM-Kommission 2011)

Collective	Aniline [µg/l urine]					Reference
	Mean	Median	95 th perc.	Range	LOD/ LOQ	
Germany						
856 NS, 145 S; 411 ♂, 592 ♀	S: 4.76 NS: 5.16	S: 3.28 NS: 2.99	S: 13.46 NS: 14.49	0.05–384.04	n. s./ 0.1	Kütting et al. 2009
8 ♂ NS; 8 ♂ S	S: 1.4 (SD: 1.5) NS: 0.2 (SD: 0.4)	S: 1.1 NS: n. d.	n. s.	S: n. d.–5.1 NS: n. d.–1.2	1/ n. s.	Riffelmann et al. 1995
81 NS; 33 ♂, 48 ♀	4.58 (AM) 2.29 (GM)	1.88	10.9	0.5–130	n. s./ 0.00312	Seidel 2005
115 NS, 45 S, 37 ShS; ♂, ♀ n. s.	n. s.	S: 3.7 NS: 3.7 ShS: 3.6	S: 7.5 NS: 8.2 ShS: 6.5	S: 1.1–9.2 NS: 0.4–13.0 ShS: 0.8–8.2	0.05 (calculated)/ 0.4	Weiß 2005

Tab. 2 (continued)

Collective	Aniline [μg/l urine]					Reference
	Mean	Median	95 th perc.	Range	LOD/ LOQ	
USA						
33 non-exposed workers from a factory with o-toluidine and aniline; NS, S status n. s.; ♂, ♀ n. s.	n. s.	2.0–3.2	n. s.	n. s.	1.4/ n. s.	Brown et al. 1995
15 NS; 7 ♂, 8 ♀	6.57	6.0	13.74	1.2–50.6	0.1/ n. s.	Chinthakindi and Kannan 2022
10 ♂ (12 samples) S, 9 ♂ (15 samples) NS	S: 3.1 ± 2.6 ^(c) NS: 2.8 ± 2.5 ^(c)	n. s.	n. s.	S: n. q.–8.8 ^(c) NS: 0.02–8.4 ^(c)	50–100 ng/24h/ n. s.	el-Bayoumy et al. 1986
31 non-exposed workers; S, NS status n. s.; ♂, ♀ n. s.	2.7 ± 2.4 ^(a) ; 3.8 ± 2.7 ^(b)	n. s.	n. s.	n. s.	1.4	Teass et al. 1993
16 NS, 10 S; 22 ♂, 4 ♀	S: 4.2 (SD: 3.1) ^(a) 6.2 (SD: 2.9) ^(b) NS: 1.6 (SD: 1.1) ^(a) 2.6 (SD: 1.8) ^(b)			n. s.		Ward et al. 1996

a) pre-shift

b) post-shift

c) [$\mu\text{g}/24\text{h}$]

AM: arithmetic mean; GM: geometric mean; LOD: limit of detection; LOQ: limit of quantification; n. d.: not detectable; n. q.: not quantifiable due to an interfering peak; n. s.: not specified; NS: non-smoker; S: smoker; SD: standard deviation; ShS: secondhand smoker

In a study of 300 pregnant women (244 non-smokers, 56 smokers) conducted in Brazil to determine the levels of aromatic amines in urine, the following concentrations of aniline in urine were reported: median: 1.38 μg aniline/l; mean: 11.73 μg aniline/l; 25th percentile: 0.89 μg aniline/l; 75th percentile: 2.87 μg aniline/l; minimum: 0.48 μg aniline/l; maximum: 218.84 μg aniline/l (Souza et al. 2023).

Between 2008 and 2020, 45 different chemicals were measured in the urine of 171 pregnant women in the USA. Aniline was detected in all urine samples: geometric mean: 0.81 μg aniline/l; median: 0.74 μg aniline/l; 25th percentile: 0.52 μg aniline/l; 75th percentile: 1.1 μg aniline/l; minimum: 0.15 μg aniline/l; maximum: 34 μg aniline/l (Choi et al. 2022).

Evaluation of a biological reference value (BAR)

Based on the available studies from Kütting et al. (2009), Weiß (2005), Seidel (2005) and Chinthakindi and Kannan (2022), a weighted mean value of the 95th percentile is calculated as 13.3 μg aniline/l urine. For this reason, a

BAR of 15 $\mu\text{g/l}$ urine

is derived for aniline. The BAR applies to both smokers and non-smokers, as the urinary concentrations did not vary significantly between these groups. Sampling time is at the end of exposure or the end of the shift.

Interpretation

The BAR is based on normally concentrated urine for which the creatinine concentration should lie within a range of 0.3–3 g/l. For urine samples outside of the aforementioned range, it is generally recommended to repeat measurement with normally hydrated subjects (translated in Bader et al. 2016).

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

The views expressed in these publications are those of the individual authors acting in their personal capacity as experts and do not represent the positions of their respective institutions or employers.

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