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Naphthalene

Assessment Values in Biological Material – Translation of the German version from 2016

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Keywords: naphthalene; tar camphor; coal tar camphor; biological reference value; BAR; background exposure

Citation Note: Klotz K, Drexler H, Hartwig A, MAK Commission. Naphthalene. Assessment Values in Biological Material – Translation of the German version from 2016. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2018 Apr;3(2):860-877]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2026. https://doi.org/10.34865/bb9120e2218_w

Republished (online): 06 Mar 2026

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.bb9120e2218

Manuscript completed: 20 Feb 2015

Published (online): 24 Apr 2018

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

Naphthalene

BAT Value Documentation

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DOI: 10.1002/3527600418.bb9120e2218

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated a BAR ("Biologischer Arbeitsstoff Referenzwert") for naphthalene, considering 1- and 2-naphthol in urine to characterize the internal exposure. Naphthalene is classified in category 2 for carcinogenic substances and designated with an "H" because of its contribution to the toxicological hazards due to penetration through the skin in vitro and dermal absorption in vivo.

In a number of biomonitoring studies, the excretion of 1- and 2-naphthol in urine of persons occupationally not exposed to naphthalene was examined. Tobacco smoking affects the naphthol excretion significantly, thus non-smokers and smokers have to be considered separately. Up to now, no data of representative collectives of the German general population are available. Therefore, the largest German study was considered for the evaluation, where urine samples of 95 non-smokers were analysed and a 95th percentile for the sum of 1- and 2-naphthol (after hydrolysis) of 33.6 µg/l (30.6 µg/g creatinine) was found. These results are in good accordance with other national and international studies. Therefore, a BAR of 35 µg 1- plus 2-naphthol (after hydrolysis)/l urine was evaluated for non-smokers. Sampling time is at the end of exposure or the end of the working shift and after long term exposure at the end of the working shift after several shifts. For the interpretation of the result, the smoking status of the persons has to be considered. In case of an occupational co-exposure to other polycyclic aromatic hydrocarbons (PAH), the analysis of additional PAH-metabolites is recommended (see MAK Documentation "Polycyclic Aromatic Hydrocarbons").

Keywords

Naphthalene; tar camphor; coal tar camphor; occupational exposure; biological tolerance value; toxicity; BAT value; BAR ("Biologischer Arbeitsstoff-Referenzwert")

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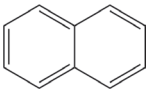
Naphthalene

BAR (2015)	**35 µg 1- plus 2-Naphthol (after hydrolysis)/l urine***
	Sampling time: end of exposure or end of shift; for long-term exposures: at the end of the shift after several shifts
MAK value	**not established**
Peak limitation	–
Absorption through the skin (2001)	H
Sensitization	–
Carcinogenicity (2001)	Carcinogen Category 2
Embryotoxicity	–
Germ cell mutagenicity (2001)	Category 3B
Synonyms	Tar camphor Coal tar camphor
CAS number	[91-20-3]
Formula	 $C_{10}H_8$
Molecular weight	128.16 g/mol
Melting point	80.2 °C
Boiling point	218 °C
Solubility in water at 20 °C	32 mg/l
Density at 20 °C	1.16 g/cm³
	1 ml/m³ (ppm) ≙ 5.327 mg/m³

* derived for non-smokers

Naphthalene is a bicyclic aromatic hydrocarbon belonging to the group of polycyclic aromatic hydrocarbons (PAHs). It is produced by the incomplete combustion of organic material as a result of many processes such as forest fires or volcanic eruptions, in the household from heating and cooking, in road and air traffic, on smoking tobacco, and by industrial processes such as hard coal coking, steel production, energy supply and waste incineration, so that it is ubiquitous in the environment (BUA 1989; IARC 2002).

In industry, naphthalene is mainly used in the synthesis of chemicals (EU 2007), but also as pore generator in the manufacture of ceramic grinding wheels (Ziener 2012).

Naphthalene is a component in creosote, a coating agent containing tar used as a preservative for wood in railway sleepers and masts as well as for the impregnation of tar paper as roofing material (EU 2007).

1 Metabolism and Toxicokinetics

1.1 Absorption, distribution and elimination

The absorption of naphthalene is mainly by inhalation (EU 2007; NTP 1992, 2000), but also through ingestion (Bock et al. 1979; Eisele 1985) and through the skin (Turkall et al. 1994). Whereas, in animal studies, absorption was 22% to 73% after inhalation, up to 93% after ingestion and more than 76% after absorption through the skin, no studies with humans have become available to date.

For elimination of the substance, studies with different mammalian species are available. After oral administration of ^{14}C-labelled naphthalene to rats in a feeding study, up to 84.3% of the dose in the urine and 6.7% in the faeces could be recovered within 72 hours (Bakke et al. 1985). Depending on the experiment 39% or 26% of the dose was metabolized to thioether derivatives and excreted with the urine. In contrast, in studies with rhesus monkeys and chimpanzees, no naphthalene thioether metabolites were detected in the urine after oral naphthalene administration of 200 mg/kg body weight. This indicates that, in these primates, glutathione conjugation either does not occur at all or only to a very slight extent (Rozman et al. 1982; Summer et al. 1979).

After dermal exposure of rats to ^{14}C-labelled naphthalene, 70% to 87% of the dose was excreted with the urine and 2% to 4% with the faeces (Turkall et al. 1994).

To date, only a few studies are available for the elimination kinetics in humans. As biomarkers for a naphthalene exposure, the metabolites 1- and 2-naphthol have mainly been analysed. After inhalation exposure to naphthalene of workers in naphthalene oil distillation, the maximum excretion of 1-naphthol was found to be one hour after the end of the shift. For the elimination of metabolites in these workers, a half-life of four hours and a mean excretion rate of 570 µg/hour was calculated (Bieniek 1994). Heikkilä et al. (1995) observed a biphasic course of the urinary 1-naphthol excretion of humans after occupational exposure to creosote. Whereas, in phase 1, a biological half-life of one to two hours was observed, this is between 14 and 46 hours in phase 2 (Heikkilä et al. 1995).

1.2 Metabolism

Various reviews and monographs are available for the metabolism of naphthalene (Buckpitt et al. 2002; Greim 1995, 2001; IARC 2002; Preuss et al. 2003).

Principally, naphthalene is first converted by oxidation into the reactive 1,2-epoxide, which is then metabolized into further metabolites, some of which are highly reactive; these are then detoxified by conjugation with glucuronic acid, sulfate or glutathione before final elimination (Greim 1995).

In total, more than 30 different naphthalene metabolites have been identified in the urine of mammals (Horning et al. 1980; Kanekal et al. 1990, 1991). Between mice, rats and humans, clear differences exist in the enzyme patterns and in the naphthalene metabolism in the target tissues (Buckpitt et al. 2002).

The main pathways of the mammalian naphthalene metabolism are given in Figure 1 as simplified illustration. As primary metabolites of naphthalene, the 1,2-epoxides naphthalene 1S,2R-oxide and naphthalene 1R,2S-oxide are formed by cytochrome P450 oxidases. The epoxides are highly reactive intermediates, for which half-lives of 10 minutes in blood and plasma (Tsuruda et al. 1995) or up to 11 minutes in the presence of albumin (Buckpitt et al. 2002; Kanekal et al. 1991) are given. Starting with naphthalene 1,2-oxide (see Figure 1, No. 1) further metabolization occurs via the following pathways (the numbers correspond to those of the metabolism scheme shown in Figure 1):

- Spontaneous conversion to 1- and 2-naphthol (2, 3) and subsequent conjugation to glucuronic acid and sulfate conjugates (4, 5)
- Conversion to 1,2-dihydroxy-1,2-dihydronaphthalene (dihydrodiol) by epoxide hydrolases (8)
- Conjugation with glutathione and further conversion to mercapturic acids (13)

A further CYP oxidation of 1,2-dihydrodiol or 2-naphthol generates 1,2-dihydroxynaphthalene (1,2-DHN, (9)); the oxidation of 1-naphthol leads to 1,4-dihydroxynaphthalene formation (1,4-DHN, (6)) (Waidyanatha et al. 2002). 1,2- and 1,4-DHN can be eliminated in free form or as glucuronide- and sulfate conjugates (11) or be oxidized to the corresponding quinones 1,2-naphthoquinone (10) and 1,4-naphthoquinone (7) (Bakke et al. 1985; Horning et al. 1980; Klotz et al. 2011; Turkall et al. 1994; Wu et al. 2005). The naphthoquinones are highly reactive and are under discussion as the ultimate carcinogens in the naphthalene metabolism. They can bind to macromolecules such as proteins and the DNA (Bolton et al. 2000; Buckpitt and Warren 1983; Cho et al. 1994; Troester et al. 2002; Tsuruda et al. 1995; Waidyanatha et al. 2002, 2004; Zheng et al. 1997).

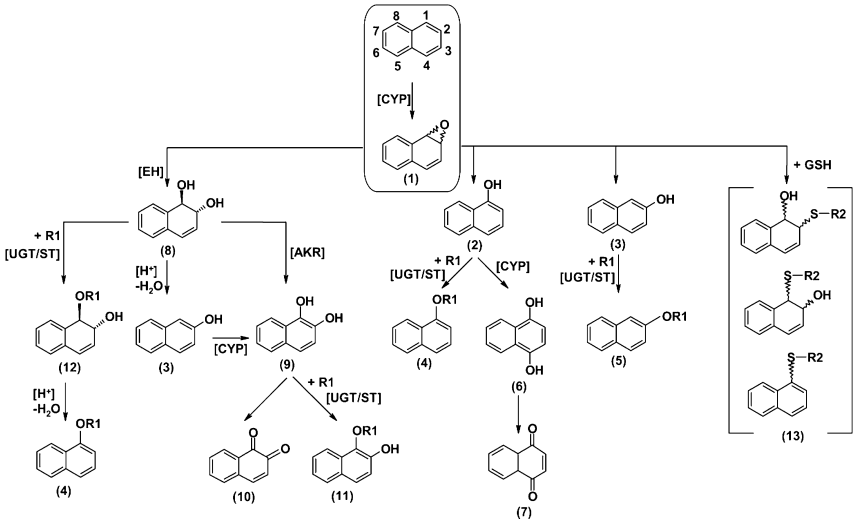


Figure 1 Naphthalene metabolism in mammals (Preuss et al. 2003)

(1) Naphthalene 1,2-epoxide
(2) 1-Naphthol
(3) 2-Naphthol
(4) 1-Naphthylglucuronide/-sulfate
(5) 2-Naphthylglucuronide/-sulfate
(6) 1,4-Dihydroxynaphthalene
(7) 1,4-Naphthoquinone
(8) trans-1,2-Dihydro-1,2-dihydroxynaphthalene
(9) 1,2-Dihydroxynaphthalene
(10) 1,2-Naphthoquinone
(11) 2-Hydroxynaphthyl-1-glucuronide/-sulfate
(12) trans-1,2-Dihydro-2-hydroxynaphthyl-1-glucuronide/-sulfate
(13) Naphthylmercapturic acids
Abbreviations: UGT/ST = UDP-glucuronyl transferase/sulfotransferase; AKR = aldo-keto reductase; CYP = cytochrome P450 oxidase; EH = epoxide hydrolase; GSH = glutathione; R1 = glucuronic acid-/sulfate residue; R2 = N-acetyl-L-cysteine residue

2 Critical Toxicity

For the toxicity of naphthalene the reader is referred to the MAK Documentations and the monographs published by various organizations (BUA 1989; Greim 1995, 2001; IARC 2002; SCOEL 2010).

In animal studies, the respiratory tract, the eyes and the haematopoietic system are the target tissues of naphthalene toxicity (Abdo et al. 2001; Shopp et al. 1984; Van Heyningen 1979; Zheng et al. 1997).

In rats and mice, tumours in the respiratory and olfactory epithelia and lung carcinomas were found (NTP 1992, 2000). The precise mode of action of naphthalene in the nasal epithelium is still not clear, though indications for a non-genotoxic mechanism exist (Clewell et al. 2014; SCOEL 2010).

In humans, after acute poisoning through swallowing mothballs containing naphthalene, as well as after inhalation, oral or dermal absorption of pharmaceuticals containing naphthalene, symptoms such as nausea, vomiting, convulsions and diarrhoea were observed, frequently accompanied by disturbed awareness, lethargy and ataxia (BUA 1989).

Parallel to this, especially haemolytic anaemia, but also sensitization and very rarely cataracts were described (Mackell et al. 1951; Melzer-Lange and Walsh-Kelly 1989; Shannon and Buchanan 1982; Todisco et al. 1991; Valaes et al. 1963; Van Heyningen and Pirie 1967; Zuelzer and Apt 1949). Haemolytic anaemia from naphthalene metabolites occurs particularly in newborn children, foetuses and persons from ethnic groups with inherited glucose-6-phosphate dehydrogenase deficiency (Lau et al. 2006).

3 Exposure and Effects

3.1 Relationship between external and internal exposure

After occupational exposure to naphthalene or PAHs at the workplace, the internal exposure of the workers can markedly increase. A review by Preuss et al. (2003) provides an overview of different studies in which the concentrations of naphthalene in the air and the 1- and 2-naphthol levels in urine at different workplaces such as in creosote production, in coking plants as well as in the production of mothballs, naphthalene and phthalic acid anhydride, were analysed.

When investigating the relationship between exposure to naphthalene in the workplace air and the respective internal 1- and 2-naphthol exposure of exposed workers, contradictory reports have been published. Whereas, in one study, a linear relationship could be demonstrated (Bieniek 1998), no relationship could be found in other studies (Kuusimäki et al. 2004; Preuss et al. 2005). Serdar et al. (2004) describe a supralinear relationship, in which, with increasing naphthalene exposure in the air, the naphthol excretion increases only to a lesser extent.

3.2 Relationship between internal exposure and effects

There are no data available to date.

4 Selection of Indicators

As indicators of an internal naphthalene exposure in humans the following parameters have been considered up to now:

- 1- and 2-naphthol in urine
- 1,2-dihydroxynaphthalene in urine
- albumin adducts of 1,2- and 1,4-naphthoquinone in blood

As further biomarker, the determination of non-metabolized naphthalene in urine has been proposed (Fustinoni et al. 2010; Rossella et al. 2009; Serdar et al. 2003 a;

Sobus et al. 2009). Compared with the naphthols, however, markedly lower naphthalene concentrations are detectable in urine, and the elimination time is shorter (Serdar et al. 2003 a). Up to now, naphthyl mercapturic acids in urine have been detected as metabolites in animal experiments only (Bakke et al. 1985; Pakenham et al. 2002).

Most of the data are available for the 1- and 2-naphthol concentrations in urine. Therefore, and for reasons of practicability, 1- plus 2-naphthol has been selected as parameter.

5 Methods

When analysing 1- and 2-naphthol in urine, an enzymatic or acidic hydrolysis of the urine samples to cleave the glucuronide and sulfate conjugates is carried out first, followed by detection using different analytical procedures. For the simultaneous quantification of 1- and 2-naphthol, methods using HPLC fluorescence (Elovaara et al. 2003; Kuusimäki et al. 2004; Preuss 2005) and GC-MS (Bouchard et al. 2001; Hill Jr et al. 1995; Li et al. 2006; Petropoulou et al. 2006; Serdar et al. 2003 b; Yang et al. 1999) are used. By the Commission, tested analytical methods for the determination of 1- and 2-naphthol in urine during human biomonitoring have been published (Hardt et al. 2010; Preuss et al. 2010).

Procedures using GC-MS after enzymatic hydrolysis have been described for the analysis of dihydroxy naphthalenes (Klotz et al. 2011; Wu et al. 2005).

For a biochemical effect monitoring in humans, a method to determine the albumin adducts of 1,2- and 1,4-naphthoquinone in blood has been published. These adducts have been detected in coke workers and controls, whereas no naphthalene-1,2-oxide adducts were found (Waidyanatha et al. 2004).

6 Background Exposure

Data on the urinary naphthol excretion of smokers and non-smokers not occupationally exposed to naphthalene are shown in Table 1. Mainly, concentrations of < 30 µg/l for 1-naphthol and < 20 µg/l for 2-naphthol were published for non-smokers, concentrations of < 45 µg/l for 1-naphthol and < 55 µg/l for 2-naphthol for smokers.

To estimate the background exposure of not occupationally exposed non-smokers, the mean value of the 95th percentile from different studies is used (see Table 2). The 95th percentiles are either given in the studies or are calculated from the sum of the mean value plus twice the standard deviation. Values related to creatinine were calculated in µg/l (1 µg/g creatinine corresponding to 1.2 µg/l). An average 95th percentile of 19 µg/l is obtained for 1-naphthol and of 15 µg/l for 2-naphthol.

Table 1 Concentrations of 1- and 2-naphthol in the urine of persons without occupational PAH exposure

Reference	n	1-Naphthol median (P95)	2-Naphthol median (P95)	Σ (1+2)-Naphthol median (P95)	Remarks
Non-smokers					
Preuss 2005	95	3.4 (18.1) µg/l 3.5 (18.4) µg/g	3.6 (17.6) µg/l 3.4 (15.5) µg/g	8.4 (33.9) µg/l 7.9 (30.6) µg/g	values for NSmo, total collective n = 124, 10–64 years, n = 5 < 18 years
Hölzer and Wilhelm 2006[##]	67	3.6 (29.9) µg/l	2.1 (16.9) µg/l		NSmo, ♀, morning urine, 25–51 years, non-exposed control collective
Hölzer and Wilhelm 2006[##]	48	2.6 (24.0) µg/l	2.0 (21.9) µg/l		NSmo, ♀, morning urine, 25–51 years, residents living in the vicinity of a coke factory showing no difference to the general population in the context of 1-naphthol
Hardt et al. 2006	50	1.0 (max 18) µg/l	1.0 (max 28) µg/l		values for NSmo, total collective n = 57
Bouchard et al. 2001	26	1.28 (8.73) µg/g	1.24 (6.41) µg/g	2.49 (15.06) µg/g	Canada, morning urine, NSmo
	28	3.39 (10.71) µg/g	2.60 (6.30) µg/g	6.20 (15.42) µg/g	Canada, morning urine, residents living in the vicinity of a creosote impregnation plant
Yang et al. 1999	56	GM 3.0 µg/l	GM 1.1 µg/l		Japan, ♂, 20–71 years
Kamal et al. 2014	34	0.8 (range 0.3–1.2) µg/g	0.8 (range 0.5–1.6) µg/g		Pakistan, m, NSmo, 28–57 years, controls without environmental PAH exposure

Table 1 (continued)

Reference	n	1-Naphthol median (P95)	2-Naphthol median (P95)	Σ (1+2)-Naphthol median (P95)	Remarks
Kuusimäki et al. 2004	46		1.7 µg/g AM 3.2 ± 4.8 µg/g[#]		winter, NSmo, 25–61 years (mean 49 years)
	38		2.9 µg/g AM 3.3 ± 2.6 µg/g[#]		summer, NSmo, 25–61 years
Kim et al. 2001	62		1.6 (7.0) µg/g		Korean students, ♂, NSmo, 23.1 ± 3.6 years
Nan et al. 2001	87		GM 2.0 ± 2.8 µg/g ~		Korean students, 40 ♂, 47 ♀
Buratti et al. 2007	12		8.0 (range 3.5–42) µg/l AM 10.6 ± 10.9 µg/l[#]		road workers without bitumen exposure prior to shift, 22–75 years, ♂
Sul et al. 2012	4 089		GM 2.8 (CI 2.6–3.0) µg/l		20–79 years; ♂ and ♀, Korea National Survey for Environmental Pollutants
Smokers					
Preuss 2005	29	19.8 (44.8) µg/l 16.6 (32.9) µg/g	19.2 (51.4) µg/l 17.4 (38.4) µg/g	40.3 (93.6) µg/l 38.1 (72.3) µg/g	values for Smo, total collective n = 124, 10–64 years, n = 5 < 18 years
Hölzer and Wilhelm 2006[##]	35	13 (32.9) µg/l	17 (52) µg/l		Smo, ♀, morning urine, 26–44 years, residents living near a coke factory and non-exposed control collective, without any difference with regard to naphthol
Hardt et al. 2006	7	4.9 (max 16) µg/l	11 (max 69) µg/l		values for Smo, total collective n = 57
Yang et al. 1999	63	GM 8.3 µg/l	GM 7.8 µg/l		♂, Japanese, 20–71 years
Kim et al. 2001	67		5.1 (11.1) µg/g		Korea, students, ♂, Smo, 23.8 ± 3.3 years

Table 1 (continued)

Reference	n	1-Naphthol median (P95)	2-Naphthol median (P95)	Σ (1+2)-Naphthol median (P95)	Remarks
Nan et al. 2001	41		GM 5.0 ± 2.4 µg/g ~		Korean students, ♂
Buratti et al. 2007	25		13.8 (range 4.5–90) µg/l AM 17.2 ± 16.7 µg/l[#]		road workers without bitumen exposure prior to shift, 22–75 years, ♂
Sul et al. 2012	613		GM 11.7 (CI 10.2–13.1) µg/l		20–79 years, ♂ and ♀, Korea National Survey for Environmental Pollutants
Bieniek 1994	24	GM 130 ± 1868 µg/l			♂, Smo
Non-smokers and smokers					
Preuss 2005	124	5.4 (29.2) µg/l	5.5 (34.0) µg/l	11.9 (70.9) µg/l	10–64 years, n = 5, < 18 years
Ziener 2012	19			8.3 (< QL–36) µg/g	10 NSmo, 9 Smo; QL for 1-naphthol: 1 µg/l QL for 2-naphthol: 2 µg/l
Hill Jr et al. 1995	983/977 (1-N/2-N)	4.4 (43) µg/l 3.4 (36) µg/g	3.4 (30) µg/l 2.6 (18) µg/g		20–59 years, USA, NHANES III
CDC 2009	1528/1515 (1-N/2-N)	2.65 (29.4) µg/l 2.52 (24.2) µg/g	3.18 (26.6) µg/l 2.91 (21.8) µg/g		USA (Survey 2003/2004, age > 20 years)
CDC 2014	1739/1768 (1-N/2-N)	2.26 (33.0) µg/l 2.36 (27.9) µg/g	3.68 (28.6) µg/l 3.47 (22.7) µg/g		USA (Survey 2007/2008, age > 20 years)
Yang et al. 1999	119	GM 5.1 (< 0.3–473) µg/l	GM 3.2 (< 0.3–189) µg/l		♂, Japanese, 20–71 years
Serdar et al. 2003 b	22	GM 4.0 ± 2.5 µg/l ~	GM 4.2 ± 2.5 µg/l ~		China, office workers, 19 NSmo, 3 Smo

Table 1 (continued)

Reference	n	1-Naphthol median (P95)	2-Naphthol median (P95)	Σ (1+2)-Naphthol median (P95)	Remarks
Eom et al. 2013	140		GM 3.49 (CI: 2.83–4.29) µg/g		controls from Korean multicenter cancer cohorts (68.9 ± 6.9 years)
Kim et al. 2001	129		2.9 (10.7) µg/g		Korea, ♂, 62 NSmo, 67 Smo, 23.5 ± 3.5 years
Nan et al. 2001	128		GM 2.7 ± 3.0 µg/g~		Korean students, 81 ♂, 47 ♀, 87 NSmo, 41 Smo

Abbreviations:
NSmo = non-smokers; Smo = smokers; n = number; P95 = 95th percentile; AM = arithmetic mean; GM = geometric mean; max = maximum; µg/g = µg/g creatinine; QL = quantification limit; CI = 95% confidence interval;
[#] AM ± SD = arithmetic mean and standard deviation
~GM ± GSD = geometric mean and geometric standard deviation
[##] cited from UBA 2007
calculated as: 1 µmol/mol creatinine = 1.27 µg/g creatinine

Table 2 Urinary excretion of 1- and 2-naphthol (95th percentile) of persons (non-smokers) without occupational PAH exposure (data partly calculated, see Table 1 for original data)

Reference	n	1-Naphthol 95th percentile [µg/l]	2-Naphthol 95th percentile [µg/l]
Preuss 2005	95	18.1	17.6
Hölzer and Wilhelm 2006##	67	29.9	16.9
Hölzer and Wilhelm 2006##	48	24.0	21.9
Bouchard 2001	26	10.5#	7.7#
Bouchard 1995	28	12.9#	7.6#
Kuusimäki et al 2004	46		15.4#
Kuusimäki et al. 2004	38		10.2#
Kim et al. 2001	62		8.4#
Nan et al. 2001	87		9.1#
Sul et al. 2012	4089		15.8
Buratti et al. 2007	87		32.4#
Mean value		**19.1**	**14.8**

calculated value
cited from UBA 2007

Only a few data are available for the background exposure to 1,2-dihydroxynaphthalene. For a collective of 21 Chinese office and hospital employees (18 non-smokers, 3 smokers), Wu et al. (2005) gave a geometric mean value of 38.8 ± 2.31 µg/l urine (Wu et al. 2005). A control collective of 29 persons in Germany was found to have clearly lower levels. In the median (range), concentrations of 4.6 µg/l (< 1.0 µg/l–19.3 µg/l) were determined in the urine for 20 non-smokers and 17.1 µg/l (1.9–62.0 µg/l) for nine smokers (Klotz et al. 2011).

Albumin adducts of 1,2- and 1,4-naphthoquinone were detected in the blood of coke workers and controls. In the median, workers were found to have significantly higher levels of 1,2-naphthoquinone albumin adducts at 77 pmol/g than the controls at 45 pmol/g, though no difference could be found for 1,4-naphthoquinone albumin adducts (workers 49 pmol/g, controls 44 pmol/g) (Waidyanatha et al. 2004). In a study by Lin et al. (2014), 1,2- and 1,4-naphthoquinone albumin adducts were detected in the serum of pregnant Taiwanese women after environmental exposure to PAHs. In the serum albumin, median adduct concentrations of 249–390 pmol/g were measured for 1,2-naphthoquinone and of 16–25 pmol/g for 1,4-naphthoquinone.

7 Evaluation

The biological reference value ("Biologischer Arbeitsstoff-Referenzwert", BAR) describes the background exposure for a reference population consisting of persons of working age not occupationally exposed to PAHs. Due to the strong influence of smoking habits on naphthol excretion, smokers and non-smokers are to be evaluated separately. For Germany, no representative population studies are available. In a

study with 124 persons not occupationally exposed to naphthalene, a 95th percentile of 33.9 µg/l urine (or 30.6 µg/g creatinine) in 95 non-smokers was given for the sum of 1- and 2-naphthol excretion. In the total of 124 investigated persons aged between 10 and 64 years, five were younger than 18 years (Preuss 2005). In other German studies, higher 95th percentiles of 29.9 or 24.0 µg/l for 1-naphthol as well as 16.9 or 21.9 µg/l for 2-naphthol (see Table 1) were given for female non-smokers in the general population (Hölzer and Wilhelm 2006).

In Canadians, Bouchard et al. (2001) determined clearly lower 95th percentiles of 15.06 or 15.42 µg/g creatinine for the sum of 1- and 2-naphthol.

In the USA, in environmental surveys by the Center for Disease Control (CDC 2014), data for the 1- and 2-naphthol excretion of 1739 or 1769 persons were published, however without distinguishing between smokers and non-smokers. At 2.26 (33.0) µg/l for 1-naphthol and 3.68 (28.6) µg/l for 2-naphtol, the medians (95th percentiles) are somewhat lower than those found in the German studies by Preuss (2005) and Ziener (2012) when evaluating smokers and non-smokers together.

For the derivation of a BAR, only data of not occupationally exposed non-smokers are used. When taking into account the data from various international studies (Bouchard et al. (2001), Buratti et al. (2007), Hölzer and Wilhelm (2006), Kim et al. (2001), Kuusimäki et al. (2004), Nan et al. (2001), Preuss (2005) and Sul et al. (2012)), 95th percentiles of 19 µg 1-naphthol (after hydrolysis)/l urine and 15 µg 2-naphthol (after hydrolysis)/l urine are obtained.

As the largest German collective of non-smokers was investigated by Preuss (2005), this study is used here for the evaluation of a BAR. Accordingly a

BAR of 35 µg 1- plus 2-naphthol (after hydrolysis)/l urine

is established **for non-smokers**.

Sampling is carried out at the end of exposure or the end of shift, and for long-term exposures: at the end of the shift after several shifts.

8 Interpretation of Data

Tobacco smoking significantly affects the naphthol excretion, which means that the smoking status of those investigated must be known in order to interpret the results.

The level of an occupational naphthalene exposure can be established by determining the naphthalene metabolites before and after the shift.

The BAR for 1- plus 2-naphthol relates to normally concentrated urine, in which the creatinine concentration should be in the range of 0.3–3 g/l. In addition to this, the Commission considers it useful, for further improving the validity of the analyses, to select a narrower target range of 0.5–2.5 g/l for urine samples. As a rule, where urine samples are outside the above limits, a repetition of the measurement in normally hydrated test persons is recommended (see BAT Documentation 2010).

In humans, naphthalene is metabolized to 1- and 2-naphthol in roughly comparable quantities. If the ratio between 1- and 2-naphthol is clearly different from the value of 1 (by a factor of 4 or more), the presence of an exposure source other than naphthalene must be considered (UBA 2007). If markedly increased concentrations of 1-naphthol are found, this possibly means that there was no exposure to naph-

thalene, but rather to residues of the insecticide Carbaryl (1-naphthyl-N-methylcarbamate) (Meeker et al. 2007; Petropoulou et al. 2006), or specific hair dyes containing 1-naphthol (Eskelinen et al. 1997; Wang and Kuo 1999). An increased excretion of 2-naphthol may be caused by residues of this substance, which is used as an intermediate in chemical synthesis (for example for dyes and tanning agents).

If the exposure involved is not only to naphthalene, but also to mixtures containing PAHs, the analysis of additional PAH metabolites is recommended for characterization of the exposure (see BAT Documentation "Polycyclische aromatische Kohlenwasserstoffe (PAH)" 2013).

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Accepted by the Working Group: 20 February 2015