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# 2-Naphthylamine – Addendum for re-evaluation of study results in biological material

## Assessment Values in Biological Material – Translation of the German version from 2021

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

1 *Leibniz Research Centre for Working Environment and Human Factors, TU Dortmund, Ardeystraße 67, 44139 Dortmund, Germany*

2 *Head of the working group "Assessment Values in Biological Material" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Friedrich-Alexander University (FAU) Erlangen-Nürnberg, Henkestraße 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, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, 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*

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

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## Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated 2-naphthylamine [91-59-8], considering 2-naphthylamine in urine to characterise the internal exposure.

Since the last evaluation of 2-naphthylamine, some new work has been published on the urinary excretion of 2-naphthylamine in occupationally non-exposed smokers and non-smokers. The literature added since the last evaluation also shows a heterogeneous data situation. Overall, the data situation on background exposure of occupationally non-exposed persons appears to be too heterogeneous and thus insufficient to evaluate a biological reference value (BAR) for 2-naphthylamine based on urinary excretion.

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| | |
|---|---|
| **BAR (2009, 2020)** | **not established** |
| **EKA (1994)** | **not established** |

| | |
|---|---|
| **MAK value** | – |
| Absorption through the skin (1966) | H |
| Sensitization | – |
| Carcinogenicity (1971) | Category 1 |
| Prenatal toxicity | – |
| Germ cell mutagenicity (2014) | Category 3 A |

## Re-evaluation

Since the last evaluation of 2-naphthylamine by the Commision (Nasterlack 2016), some new work has been published on the urinary excretion of 2-naphthylamine in occupationally non-exposed persons: Fuller et al. (2018) reported on ten non-smokers and 13 e-cigarette smokers, and Niu et al. (2018) reported on one non-smoker and two smokers (see Table 1). Yu et al. (2014) published a paper in which 2-naphthylamine was for the first time detected in the 24-hour urine of all subjects studied (40 smokers, 10 non-smokers). However, there was considerable variation in 2-naphthylamine excretion, particularly in the smokers. In addition to the studies described, data are available from a research report on identification of sources of nitro-/aminoarenes in the urine of nonsmokers (81, 63, and 57 non-smokers) by Seidel (2005). Table 1 shows a compilation of the available literature on persons not occupationally exposed to 2-naphthylamine.

**Tab. 1** Concentrations of 2-naphthylamine in the urine of adult persons

| Analytical method | Collective | Statistical parameters | 2-Naphthylamine in urine | | References |
|---|---|---|---|---|---|
| | | | Non-smokers | Smokers | |
| HPLC/FLD | 114 control persons from Denmark, probably ♂<br>– no data on smoking status | minimum | < 0.272 nmol/l (*< 39 ng/l*) | | Hansen et al. 1992 |
| | | maximum | 8.87 nmol/l (*125 ng/l*) | | |
| not specified | 49 control persons from Denmark, probably ♂ (controls to foundry workers)<br>– 19 non-smokers<br>– 30 smokers | AM | 0.003 µmol/mol creatinine (*4 ng/g creatinine*) | | Hansen et al. 1994 |
| GC/ECD<br>LOD = 1000 ng/l | 43 workers from Germany occupationally exposed to aniline and chloroaniline, ♂<br>– 21 non-smokers<br>– 22 smokers | AM | 2100 ± 2800 ng/l | 3900 ± 2200 ng/l | Riffelmann et al. 1995 |
| | | median | 1700 ng/l | 3900 ng/l | |
| | | maximum | 11 600 ng/l | 9800 ng/l | |
| | 16 control persons from Germany, ♂<br>– 8 non-smokers<br>– 8 smokers | AM | 500 ± 700 ng/l | 3100 ± 2100 ng/l | |
| | | median | < 1000 ng/l (LOD) | 3100 ng/l | |
| | | maximum | 1600 ng/l | 7400 ng/l | |

**Tab. 1** *(continued)*

| Analytical method | Collective | Statistical parameters | 2-Naphthylamine in urine | | References |
|---|---|---|---|---|---|
| | | | Non-smokers | Smokers | |
| GC/MS | 44 persons from Munich and surroundings, 18 ♂ and 26 ♀<br>– 32 non-smokers (of whom 21 passive smokers)<br>– 12 smokers<br>individual values from Grimmer et al. (2000); outliers eliminated according to Seidel et al. (2001) | AM | *44 ± 53 ng/24 h* | 85 ± 103 ng/24 h | Grimmer et al. 2000; Seidel et al. 2001 |
| | | median | *33 ng/24 h* | 30 ng/24 h | |
| | | 90$^{th}$ percentile | *71 ng/24 h* | 242 ng/24 h | |
| | | 95$^{th}$ percentile | *147 ng/24 h* | | |
| | | maximum | *282 ng/24 h* | 275 ng/24 h | |
| GC/MS<br>LOD = 75 ng/l | 20 random samples from 2 collectives from the representative normal population Germany | maximum | < 75 ng/l (LOD) | | Weiss and Angerer 2002 |
| GC/MS<br>LOD = 3 ng/l | 20 persons from Germany<br>– 10 non-smokers<br>– 10 smokers | AM | 10.7 ± 9.5 ng/24 h | 20.8 ± 11.2 ng/24 h | Riedel et al. 2006 |
| | | minimum | 3.7 ng/24 h | 6.2 ng/24 h | |
| | | maximum | 30.2 ng/24 h | 46.9 ng/24 h | |
| GC-MSD<br>LOQ = 0,43 ng/l | 42 of 81 non-smokers > LOD Munich | range | 0.89–232 ng/24 h | | Seidel 2005 |
| | | median | 1.1 ng/24 h | | |
| | | 95$^{th}$ percentile | 45.1 ng/24 h | | |
| | 63 non-smokers Munster | median | 7.3 ng/24 h | | |
| | 57 non-smokers Greifswald | median | 9.5 ng/24 h | | |
| LC-MS/MS | 10 non-smokers<br>40 smokers<br>China | mean value | 10.18 ± 7.25 ng/24 h | 47.40 ± 50.68 ng/24 h | Yu et al. 2014 |
| LC-MS | 10 non-smokers<br>13 smokers (e-cigarettes)<br>USA | mean value | 1130 ± 360 ng/l | 1460 ± 230 ng/l | Fuller et al. 2018 |
| | | range | 400–1690 ng/l | 1050–1760 ng/l | |
| GC-MS/MS combined with JUC-Z2-coated SPME fibre<br>LOD = 0,012 ng/l | 1 non-smoker | | n. d. | – | Niu et al. 2018 |
| | 1 smoker | | 68.4 ng/l | | |
| | 1 smoker<br>China | | 93.0 ng/l | | |

AM: arithmetic mean; GC/ECD: gas chromatography/electron capture detector; GC/MS: gas chromatography/mass spectrometry; GC-MSD: gas chromatography/mass spectrometry detector; HPLC/FLD: high-performance liquid chromatography with fluorescence detection; JUC-Z2: two-dimensional porous organic framework; LC-MS: liquid chromatography with mass spectrometry coupling; LOD: limit of detection; LOQ: limit of quantification; n. d.: not detected; SPME: solid phase microextraction; values in *italics* were calculated

The data presented in Table 1 on the background exposure of persons not occupationally exposed is too heterogeneous and thus insufficient to evaluate a biological reference value (BAR) for 2-naphthylamine based on urinary excretion.

**Therefore, no BAR for 2-naphthylamine in urine is derived.**

# Notes

## Competing interests

The established rules and measures of the commission to avoid conflicts of interest (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

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