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Antimony and its inorganic compounds – Addendum for evaluation of a BAR

Assessment Values in Biological Material – Translation of the German version from 2020

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Abstract

In 2019 the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated a biological reference value (BAR) for antimony [7440-36-0] and its inorganic compounds, considering antimony in urine to characterise the internal exposure.

A study conducted in the northern and western regions of Germany showed a 95th percentile of 0.18 µg antimony/l urine of adults from the general population (n = 87). A considerable larger study on the concentration of antimony in the urine of adults from the Belgian population (n = 1022) showed a 95th percentile of 0.236 µg antimony/l urine. The results are in good accordance, therefore, a BAR of 0.2 µg antimony/l urine was established. Sampling time for long-term exposure is at the end of the shift after several previous shifts.

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BAR (2019)	**0.2 µg antimony/l urine** Sampling time: End of exposure or end of shift; for long-term exposures: at the end of shift after several previous shifts.

Re-evaluation

In 2002, the database available for antimony and its inorganic compounds was not sufficient to set a BAT value or establish an EKA correlation as described in the BAT documentation 2003 (translated 2005, Schaller 2005). In the following addendum a biological reference value (BAR) is derived, which can be used for the evaluation of additional occupation-related exposures to antimony and its inorganic compounds.

Selection of the Indicators and Materials

In the BAT documentation (Schaller 2005), the parameters antimony in whole blood and antimony in urine for biological monitoring were assessed. Due to the longer elimination kinetics and the more convenient analytical procedure, determination of antimony in urine was preferred.

In addition to the determination of the total amount of antimony, determination of antimony species in urine was also reported (Lindemann et al. 2000; Ye et al. 2018). The latter is however not suitable for practical application at present.

Analytical Methods

An ICP-MS collection method for the determination of antimony, lead, cadmium, platinum, mercury, tellurium, thallium, bismuth, tungsten, and tin in urine was validated and published by the Commission (Schramel et al. 1999). The method description is based on the ICP Quadrupole MS technique with collision/reaction cell. During testing of the method mutual confirmation was reached with the ICP Sector Field MS technique. The studies by Heitland and Köster (2006 b), Bocca et al. (2010) and Nisse et al. (2017) show that this analytical procedure is suitable also for the matrix blood or blood plasma.

For the determination of the antimony species antimonite (Sb(III)), antimonate (Sb(V)) and trimethyl antimony dichloride in urine a procedure tested by the Commission is available which is based on the coupling of anion exchange chromatography and ICP-MS technique (Michalke et al. 2020).

Background Exposure

A study on antimony exposure was conducted in a representative sample in Germany within the framework of the Environmental Survey for Children 2003–2006 of the Federal Environment Agency (UBA 2009). The antimony concentration was determined in spontaneous urine samples of 1729 children aged 3 to 14 years, who were selected from all over Germany as representative. Of the results, 99.9% were above the limit of detection of 0.006 µg antimony/l urine. The analytical method was not specified. The range of the results was between < 0.01 µg/l and 1.0 µg antimony/l urine. The obtained median was 0.11 µg/l and the 95th percentile 0.31 µg antimony/l. Based on the results of this study, the Human Biomonitoring Commission of the German Federal Environment Agency set a reference value of 0.3 µg antimony/l urine for children aged 3 to 14 years (UBA 2009).

For the antimony exposure of adults in Germany, the results of a study by Heitland and Köster (2006 a) are available. In addition to other metals, they analysed also the antimony levels in urine samples of 87 adults from northern and western Germany not occupationally exposed to antimony using an ICP Quadrupole MS method with colli-

sion/reaction cell. The results of the analysis showed that 79% of the values were above the limit of quantification of 0.021 µg antimony/l urine. The range of the results was between < 0.021 and 0.57 µg antimony/l, the geometric mean was 0.039 µg antimony/l and the 95th percentile 0.18 µg antimony/l urine.

In another study, Heitland and Köster (2006 b) investigated, in addition to other metals, the antimony concentrations in blood samples of 130 adult persons from northern Germany. They also used the ICP Quadrupole MS technique with collision/reaction cell. Only 16% of the analytical results were above the limit of quantification of 0.013 µg antimony/l. The range of the results was between < 0.013 and 0.13 µg antimony/l urine. A geometric mean of < 0.013 µg/l and a 95th percentile of 0.040 µg antimony/l urine were determined.

In addition, there are several studies available for antimony exposure of the general population in neighbouring EU countries:

Hoet et al. (2013) also used the ICP Quadrupole MS method with collision/reaction cell to analyse, in addition to other metals, the antimony levels in the urine of 1022 adult persons from the Belgian population. Of the obtained results 65% were above the limit of detection of 0.010 µg antimony/l urine. The obtained median was 0.040 µg antimony/l urine and 0.041 µg antimony/g creatinine, respectively, and the 95th percentile was 0.236 µg antimony/l urine and 0.153 µg antimony/g creatinine, respectively.

Nisse et al. (2017) analysed the levels of various metals and metalloids including antimony, in the blood and urine of the adult general population in northern France. In this study, they also used ICP Quadrupole MS equipment with collision cell. The antimony content was detectable in 87% of the 1910 analysed urine samples. The median was 0.09 µg antimony/l urine and 0.07 µg antimony/g creatinine, respectively, and the 95th percentile 0.41 µg antimony/l urine and 0.41 µg antimony/g creatinine, respectively. In blood, antimony was detectable in 90% of the 121 samples analysed. The median was 0.06 µg antimony/l blood and the 95th percentile 0.18 µg antimony/l.

Domingo-Relloso et al. (2019) investigated the metal exposure of persons from the general population in a region in the northwest of Spain. They also used the ICP Quadrupole MS technique with collision/reaction cell. The determination of antimony in the urine samples of 1440 adults from the region yielded a median of 0.08 µg antimony/g creatinine; the 25th percentile was 0.03 µg antimony/g creatinine and the 75th percentile 0.16 µg antimony/g creatinine. No association between smoking behaviour and the antimony concentration in urine was obtained after analysing for possible determinants of the results. There was also no difference in the antimony exposure of women and men.

During their testing of analytical methods, Alimonti et al. (2005) also investigated the antimony content in the urine of 50 adult persons aged 20 to 68 years from central Italy. The analysed values were in the range from 0.011 to 0.179 µg antimony/l urine. The obtained median was 0.061 µg antimony/l, the 10th percentile was 0.024 µg antimony/l and the 90th percentile 0.119 µg antimony/l urine. In addition, the same research group investigated the antimony exposure of the general population in the two Italian regions of Umbria and Calabria using the analysis of antimony in blood plasma (Bocca et al. 2010). The technique used was ICP Sector Field MS. With this method, antimony could be detected in each analysed plasma sample. In the 291 plasma samples from Umbria the analysed values were in the range from 0.02 to 0.57 µg antimony/l. The determined median was 0.08 µg antimony/l and the 95th percentile 0.38 µg antimony/l plasma. In the 221 plasma samples from Calabria, the analysed values ranged from 0.01 to 0.29 µg antimony/l. The median was determined to be 0.09 µg/l plasma and the 95th percentile 0.22 µg antimony/l plasma.

In the United Kingdom, a working group of the British Health and Safety Executive (HSE) conducted a study to determine 61 elements including antimony in the urine of not occupationally exposed adult persons (n = 132) (Morton et al. 2014). In 20% of the analysed samples the antimony concentration was above the limit of quantification of 0.092 µg antimony/l urine. The obtained median was accordingly < 0.092 µg antimony/l. The 95th percentile was 0.26 µg antimony/l urine and 0.435 µg antimony/g creatinine, respectively.

Evaluation of the BAR

For the derivation of a biological reference value (BAR) the parameter antimony excretion in urine is especially suitable. Numerous studies are available for this parameter. For the derivation of a BAR, the study by Heitland and Köster (2006 a) with a 95th percentile of 0.18 µg antimony/l urine and the study by Hoet et al. (2013) with a 95th percentile of 0.236 µg antimony/l urine are used. Based on these data

a BAR of 0.2 µg antimony/l urine

is derived.

For long-term exposures samples should be taken at the end of the shift after several previous shifts due to the slow elimination kinetics of this parameter.

Interpretation of Data

The BAR relates to normally concentrated urine, in which the creatinine concentration should be in the range between 0.3 and 3 g/l urine. As a rule, where urine samples are outside the above limits, a repetition of the measurement in normally hydrated test persons is recommended as described in the addendum of 2011 (translated in Bader et al. 2016).

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