Addendum to Aluminium

BAT (2008)	**60 µg aluminium/g creatinine**
	sampling time: not fixed
MAK value (1997)	**1.5 mg/m³ R (respirable fraction)**
MAK value (2006)	**4 mg/m³ I (inhalable fraction)**
Absorption through the skin	–
Carcinogenicity	–

9 Re-evaluation

A biological tolerance value (BAT value) of 200 µg aluminium/l urine was established in 1989 (see Documentation 1990, translated). The BAT value was based on a linear correlation between external and internal exposure to aluminium at the MAK value of 6 mg/m³ (measured as fine dust) valid at the time. Then, in 1997, the MAK value for aluminium was established at 1.5 mg/m³ R (respirable fraction) and later, in 2006, at 4 mg/m³ I (inhalable fraction). The lowering of the MAK value now makes re-evaluation of the BAT value necessary.

9.1 Metabolism and toxicokinetics

The data on the biological half-life of aluminium eliminated via the kidneys after inhalation varies greatly in some cases. Depending on the particular exposure situation and duration these data are scattered between a few hours (Pierre et al. 1995; Sjögren et al. 1985) to weeks, months and years (Elinder et al. 1991; Letzel et al. 1999; Ljunggren et al. 1991; Sjögren et al. 1988).

In addition to considerable individual differences whose cause is still for the most part unexplained, the accumulation of aluminium in different compartments of the organism with differences in elimination behaviour possibly plays a decisive role in renal excretion kinetics (Sjögren et al. 1988). Two functional compartments, one with a relatively rapid and the other with a delayed elimination rate are being discussed; the lungs and the skeletal system are here most probably involved (ATSDR 1999; Sjögren et al. 1988).

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Furthermore, apart from individual factors, the biological half-life of aluminium elimination via the kidneys mainly seems to depend on the cumulative long-term exposure (Letzel et al. 1999).

As investigations in aluminium welders have shown, no significant differences between pre-shift and post-shift urinary excretion of aluminium under cumulative long-term exposure are to be expected due to long biological half-lives (Roßbach et al. 2006).

9.2 Exposure and effects

9.2.1 Relationship between external and internal exposure

Occupational medical investigations on the relationship between external and internal exposure are available (Letzel and Roßbach 2008; Mussi et al. 1984; Sjögren et al. 1985).

In the investigation by Mussi et al. (1984) which, among others, was the basis for the establishment of the 1989 BAT value of 200 µg/l, 7 persons exposed to aluminium were included. These were 4 aluminium welders and 3 persons exposed to dusts containing aluminium. The concentrations of aluminium dust and aluminium welding fumes determined by personal air sampling varied between 1.0 and 6.2 mg/m³. The average aluminium concentration in urine at the end of the shift was 92.7 µg/l (range 15–232 µg/l). Figure 1 shows the relationship between external and internal aluminium exposure as modified according to Mussi et al. (1984). This

$$\text{Al-U } (\mu g/l) = 29{,}6 + 25{,}0 \cdot \text{Al-L } (mg/m^3).$$

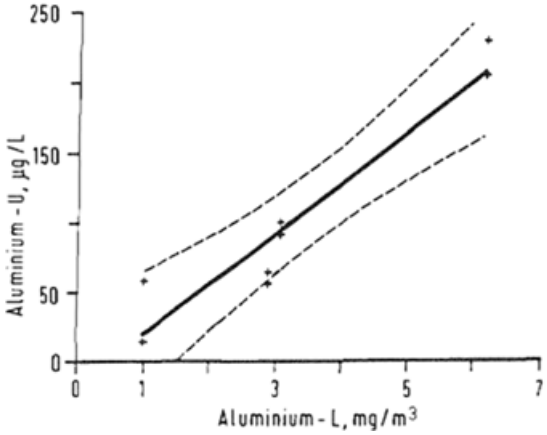

Figure 1 Relationship between external aluminium concentration in the air (aluminium-l, mg/m³) and internal aluminium exposure in urine (aluminium-U, µg/l) (see Documentation 1990, translated, data according to Mussi et al. (1984))

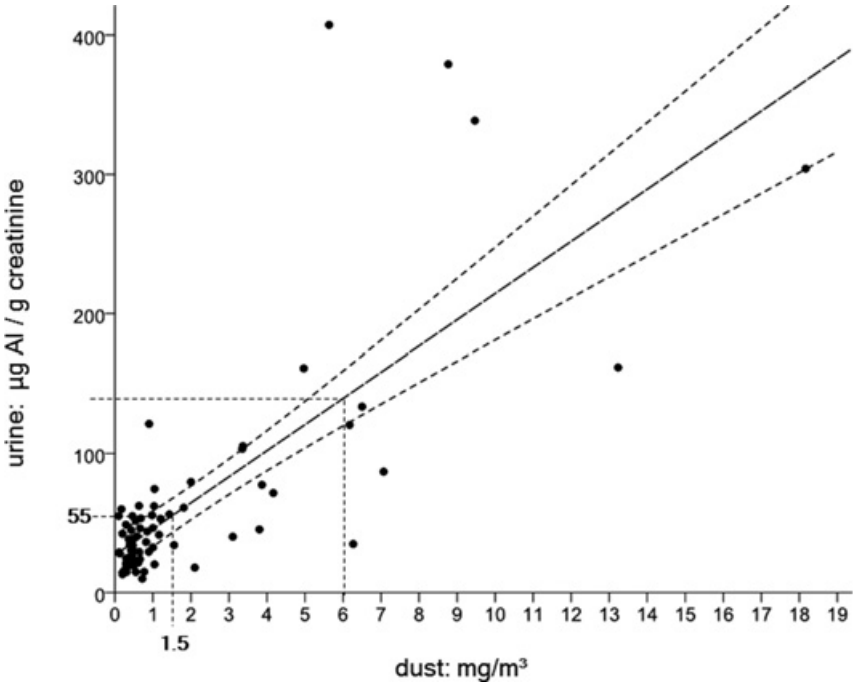

Figure 2 Relationship between total dust concentration (mg/m³) and the urinary excretion of aluminium (µg/g creatinine) in 73 aluminium welders (Letzel and Roßbach 2008)

resulted in the derivation of a BAT value of 200 µg aluminium/l urine at the time. In Figure 1, the aluminium concentrations of 6 mg/m³ (former MAK value) and 1.5 mg/m³ (present MAK value) in the air were emphasized. Accordingly, a concentration of 1.5 mg/m³ corresponds to a urinary aluminium concentration of about 50 µg/l.

According to comparable investigations by Sjögren et al. (1988), an external exposure to 6 mg aluminium/m³ results in a post-shift urinary excretion of about 180–233 µg aluminium/l. For the currently valid lower MAK value (1.5 mg/m³), aluminium excretions of about 67 to 77 µg/l are obtained according to the regression equations given by the authors.

In a longitudinal study from truck construction and train and custom vehicle construction industry (Kiesswetter et al. 2007; VMBG and HVBG 2006) aluminium welders were investigated at 2-year intervals for a total of three times. From both fields, dust measurements (total dust) and biomonitoring results were available for 73 persons. On a group basis, this investigation found that the volume-based (µg/l) urinary aluminium concentration was higher by a factor of about 1.5 compared with the creatinine-related aluminium concentration (µg/g creatinine).

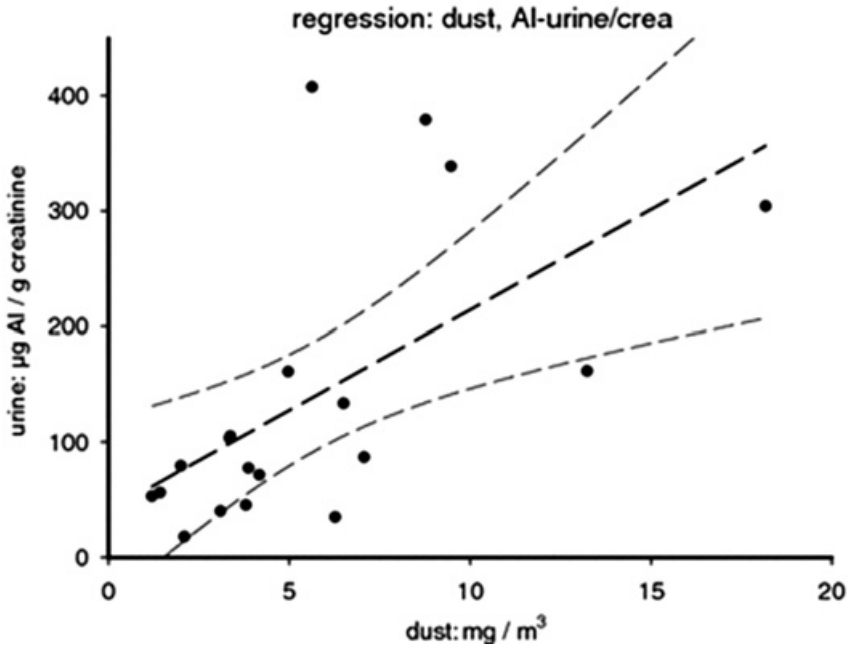

Figure 3 Relationship between total dust concentration (mg/m³) and the urinary excretion of aluminium (µg/g creatinine) in 19 aluminium welders from the train and custom vehicle construction industry (Kiesswetter et al. 2007)

Figure 2 shows the linear correlation between total dust values (as "worst-case" scenario, the total dust concentration was equated to the aluminium dust concentration) and the aluminium concentrations in urine. In this case, a total dust concentration of 1.5 mg/m³ corresponds to a urinary aluminium concentration of 55 µg/g creatinine.

After a subdivision of individuals into a higher exposed Group 1 from train and custom vehicle construction, and into a lower exposed Group 2 from truck construction, the linear correlations shown in Figure 3 and Figure 4 are obtained. A total dust concentration of 1.5 mg/m³ corresponds to an aluminium concentration in urine of 66 µg/g creatinine (train and custom vehicle construction) or of 51 µg/g creatinine (truck construction).

Altogether, the available investigations indicate that a total dust concentration of 1.5 mg/m³ corresponds to a urinary aluminium concentration in the range of about 50–66 µg aluminium/g creatinine (Letzel and Roßbach 2008).

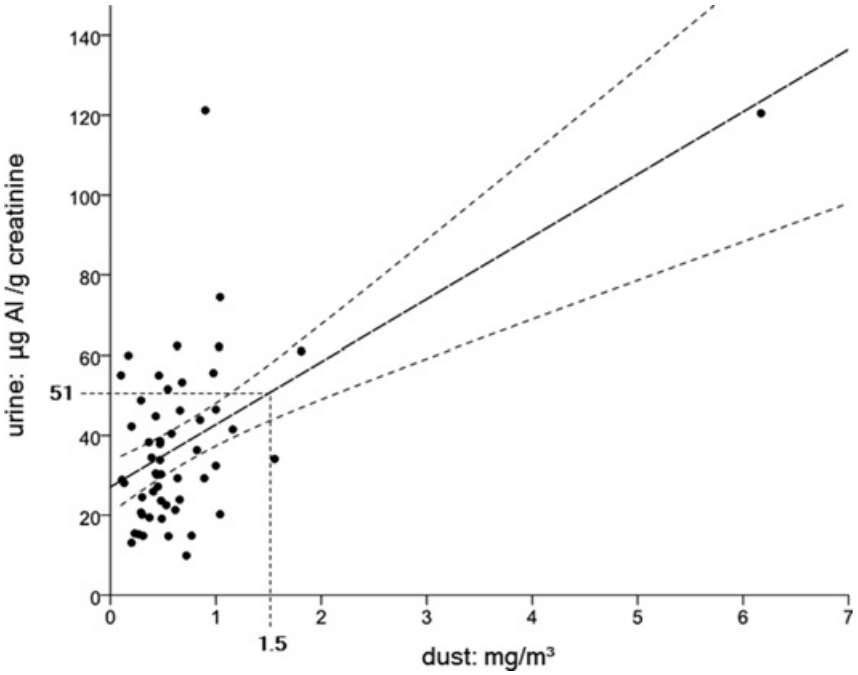

Figure 4 Relationship between total dust concentration (mg/m³) and the urinary excretion of aluminium (µg/g creatinine) in 54 aluminium welders from the truck construction industry (Letzel and Roßbach 2008)

9.2.2 Relationship between internal exposure and effects

In occupational medicine, there are clear indications for a sometimes very high internal aluminium exposure after inhalation (among others: Dehm et al. 1996; Elinder et al. 1991; Hänninen et al. 1994; Kraus et al. 1997; Letzel 1994; Letzel et al. 1996 a, b, 1999; Ljunggren et al. 1991; Röllin et al. 1991; Sjögren et al. 1988, 1996; Schlatter and Steinegger 1991; VMBG and HVBG 2006). Depending on the special exposure conditions for workers in aluminium powder production, urinary aluminium concentrations of more than 1 000 µg/l and plasma aluminium concentrations of more than 80 µg/l after inhalation are cited in the literature. These are far above the reference values for aluminium in the general population (Letzel 1994; Letzel et al. 1996 a; see Section 9.4). For some aluminium welders aluminium concentrations of more than 500 µg/l urine were found (Sjögren et al. 1988; Zhou 1996). In recent years, improvements in occupational hygiene conditions have resulted in reduced aluminium uptake from inhalation at many workplaces (Letzel et al. 1999). According to the scientific data presently available on exposure to dusts containing aluminium, the lungs and the central nervous system are considered to be the

particularly critical target organs in humans from a toxicological viewpoint. High aluminium concentrations in the air at the workplace, which in former years were frequently above the then valid MAK value of 6 mg/m^3 (respirable fraction, annual average concentration) for dust containing aluminium, produced a higher incidence of lung fibrosis, the so-called aluminosis or aluminium dust lung. The aluminium concentrations in urine observed here were above 200 µg/l urine (Greim 2007; translated). In a study in the aluminium powder production with a collective of 62 persons formerly exposed to high aluminium concentrations, radiological examination revealed early stages of aluminosis in 15 persons. Considering the internal aluminium exposure recorded at the time of diagnosis, the relative chances for developing aluminosis were significantly increased in exposed persons having a urinary aluminium concentration of > 200 µg/l (OR 9.75) or > 200 µg/g creatinine (OR 6.6) compared with those exposed to lower levels (Kraus et al. 2006). Up to the present day, however, no sufficient exposure data are available on how an aluminosis develops in order to obtain a dose-effect relationship (Greim 2007; translated).

With regard to its neurotoxic effect, it is a known fact that aluminium is able to induce encephalopathy (dialysis encephalopathy syndrome) in dialysis patients subject to a high aluminium intake from dialysates containing impurities or medication containing aluminium. In these patients, serum aluminium concentrations of < 60 µg/l are considered to be acceptable, higher values to be harmful (Consensus Conference 1993). Central nervous effects were also observed in persons subject to workplace-related aluminium exposure. However, it is not possible to evaluate these effects with any clarity due to the absence of dose-effect relationships and mixed exposure to other neurotoxic substances (Kiesswetter et al. 2007). Indications as to a possible development of Alzheimer's disease from exposure to aluminium at the workplace could not be confirmed up to now.

Up to the present, no sufficient exposure data are available to determine a dose-effect relationship for aluminosis. In addition to the level and duration of exposure, the hazard of contracting this disease is particularly high at workplaces where exposure to pounded non-greased or only weakly greased aluminium powder is present. Due to mixed exposures, both to greased and non-greased as well as pounded and ground aluminium powder in the aluminium powder industry, it is at present still not clear whether exposure exclusively to greased and ground aluminium powder can also result in lung fibrosis (Kraus et al. 1997).

High resolution computer tomography (HRCT) was used in longitudinal studies with aluminium welders in the truck construction industry as well as the train vehicle and custom vehicle construction industry. The results showed early stages of aluminium-related pulmonary fibrosis in a number of mostly high-exposed participants. In addition, emphysematous lung changes became increasingly noticeable during the observation period, whereby especially smokers and former smokers were affected. It is neither possible to determine how far occupational (aluminium and ozone among other factors) and non-occupational factors (smoking) are involved in causing the inflammatory lung changes found nor can the contribution of these individual noxae in such changes be assessed at present (VMBG and HVBG 2006).

The reader is referred to the MAK documentation for further details (Greim 2007, translated).

9.3 Selection of indicators

As already presented in the BAT documentation, serum or plasma or urinary aluminium concentrations are available as exposure parameters for monitoring exposed persons, whereby determination in urine was found to be the method of choice.

Investigations in the train and custom vehicle construction industry as well as in the truck construction industry have confirmed that no clear correlation exists between plasma aluminium concentration and total dust concentration (Letzel and Roßbach 2008). In addition it is found that the plasma aluminium concentration in occupationally exposed collectives at values below 10 µg/l is not much above that observed in the general population. The determination of plasma aluminium is thus poorly suited for objective and quantitative determination of occupational aluminium exposure. In addition, it appears that occupational aluminium uptake is more clearly reflected by its concentration in urine than by levels found in plasma (Roßbach et al. 2006). As the aluminium concentrations in urine related to creatinine show better correlations to the aluminium concentration in the air than the volume-related (Letzel and Roßbach 2008), the determination of aluminium levels in urine related to creatinine is preferred.

9.4 Background exposure

According to data by the German Human-Biomonitoring Commission (HBM) from 1998, the reference value for aluminium in plasma is < 5 µg/l and for aluminium in urine < 15 µg/l (UBA 1998). No indications of sex or age specific differences with regard to background exposure in the general population are available.

9.5 Evaluation

From the present data, no BAT value for aluminium on the basis of relationships between internal exposure and relevant effect parameters can be established. Therefore, evaluation must continue to be based on relationships between external and internal exposure. The present MAK value of 1.5 mg/m^3 here serves as a correlate. The creatinine-related urinary excretion of aluminium (µg/g creatinine) is used as biological parameter.

The investigations by Mussi et al. (1984) and Sjögren et al. (1988) already taken as basis for the BAT value established in 1989 as well as more recent studies (Letzel

and Roßbach 2008) are available for re-evaluation of the BAT value. The aluminium excretion values derived on the basis of correlations for the MAK value of 1.5 mg/m^3 are within a range of about 50–67 µg aluminium/g creatinine.

The BAT value for the excretion of aluminium in urine is therefore set at

60 µg aluminium/g creatinine.

Sampling does not have to be carried out at fixed times considering the long biological half-life after cumulative aluminium exposure.

9.6 Interpretation

The BAT value relates to normally concentrated urine, in which the creatinine content should be within the range of 0.5–2.5 g/l. As a rule, a repetition of the measurement in normally hydrated participants is recommended when urine samples are outside the given limits.

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