Nitrobenzene, Addendum

9 Evaluation of an Additional BAT Value

The MAK value for nitrobenzene established in 1958 was withdrawn in 1998 on reclassification into Category 3 of Section III of the *List of MAK and BAT Values* (Greim 1998). Attention is drawn to the subordinate importance of genotoxicity combined with a probably non-linear dose-response relationship.

The BAT value of nitrobenzene refers to the level of the haemoglobin adduct produced by nitrobenzene and is based on the Met-Hb value as typical effect parameter during occupational exposure to nitrobenzene. The BAT value derived in this way can be retained for preventive measures in occupational medicine for cases where exposure to nitrobenzene takes place.

9.1 Conclusions and Recommendations

The BAT value for nitrobenzene derived in 1986 tolerates an exposure to nitrobenzene which can lead to the formation of up to 5 % Met-Hb and correspondingly to 100 µg aniline, released from Hb adducts per litre blood. The Senate Commission of the DFG has repeatedly pointed out that, when assessing findings from haemoglobin adduct formation, its long persistence must be considered. Serum albumin has a half-life of 19 days and erythrocytes have a lifespan of 120 days (Lewalter and Neumann 1998). In the case of acute intoxications with aniline-Hb adduct findings in the range of the limit value, this must be taken into account. Acute intoxication by moderate additional exposure to nitrobenzene can already lead to a transgression of the BAT value of 100 µg aniline, released from Hb adducts/litre blood, this effect being due to the cumulative effects of long-lasting Hb adducts. As remedy, evaluation of adducts of aniline with proteins with different elimination rates has been suggested in such special cases (Lewalter and Neumann 1998).

As biochemical effect markers for exposure to nitrobenzene, the aniline adducts formed from nitrobenzene metabolism can be used both with serum albumin and with haemoglobin; the albumin adducts are degraded in vivo much more rapidly than the Hb adducts. The quotient from Hb and HSA adducts thus greatly depends on the time of measurement and increases with the time between measurement and acute exposure.

For prevention in the case of exposure to nitrobenzene, the adduct levels of the corresponding aniline with Hb and HSA can in principle be monitored. According to the previous BAT value establishment, the aniline-Hb adduct level may at the most be 100 µg released aniline per litre blood.

If increased Hb adduct values occur after acute over-exposure, the decline of the exposure can be established reliably from the albumin adduct produced. From the available time courses of concentration changes (Lewalter and Neumann 1998), an aniline-albumin adduct level of

100 µg aniline released from albumin/l blood

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is established as additional tolerance value.

Both values are not the same pathophysiologically on account of the different accumulation. General monitoring of chronic nitrobenzene exposures with the aniline-Hb adduct level is recommended and, where necessary, control of additional developments following short-term exposures with the aniline-albumin level.

10 References

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