

Concepts of Biological Limit Values (BAT Values, EKA and BLW)

The BAT Concept – Biological Tolerance Value for Occupational Exposures (Biologischer Arbeitsstoff-Toleranz-Wert)

Definition

The BAT value (“Biologischer Arbeitsstoff-Toleranz-Wert”: biological tolerance value for occupational exposures) is defined as the maximum permissible quantity of a chemical substance or its metabolites or the maximum permissible deviation from the norm of biological parameters induced by these substances in exposed humans. The BAT value is established on the basis of currently available scientific data which indicate that these concentrations generally do not affect the health of the employee adversely, even when they are attained regularly under workplace conditions. As with MAK values, BAT values are established on the assumption that persons are exposed at work for at most 8 hours daily and 40 hours weekly. BAT values established on this basis may also be applied without the use of correction factors to other patterns of working hours.

BAT values can be defined as concentrations or rates of formation or excretion (quantity per unit time). BAT values are conceived as ceiling values for healthy individuals. They are generally established for blood and/or urine and take into account the effects of the substances and an appropriate safety margin, being based on occupational medical and toxicological criteria for the prevention of adverse effects on health.

Prerequisites

By definition, BAT values can be established only for such substances which can be taken up by the body in substantial quantities via the lungs and/or other body surfaces

(skin, gastrointestinal tract) during occupational exposure. Another prerequisite for the establishment of a BAT value is that sufficient occupational-medical and toxicological data are available for the substance and that these data are supported by observations in man. The data must have been obtained with reliable methods. For the establishment of new BAT values and the annual review of the list, the submission of suggestions and reports of experience with such substances in man is requested.

Derivation of BAT Values

The derivation of a BAT value can be based on various constellations of scientific data which reveal a quantitative relationship between exposure concentration and body burden and therefore permit the linking of MAK and BAT values. These include

- studies which reveal a direct relationship between concentrations of a substance, metabolite or adduct in biological material (body burden) and adverse effects on health
- studies which reveal a relationship between a biological indicator (effect parameter) and adverse effects on health.

The following considerations of sex-specific factors apply for the establishment of BAT values:

1. The range of the variation in human anatomical and physiological differences which affect the toxicokinetics of a substance is very wide even for a single sex; the ranges for the two sexes overlap.
2. The resulting sex-specific differences in toxicokinetics vary in a range which is insignificant compared with the uncertainty involved in establishing threshold values.
3. Pregnancy can be associated with certain changes in the toxicokinetics of xenobiotics. In practice, however, the effects of these changes are limited, so that for health protection at the workplace it is the effects on the embryo and foetus which are of particular importance.

Documentation

The reasons why a BAT value was established at a particular level are documented by the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area in a loose-leaf collection entitled “Arbeitsmedizinisch-toxikologische Begründungen von BAT-Werten”. Some of these documents are available in English in the present series. They combine a critical review of the available data with comments on the values for the parameters which have been shown in practice to make a useful contribution to occupational hygiene.

Purpose

In the context of specific occupational-medical check-ups, BAT values are intended to protect employees from impairment of health at work. They provide a basis for deciding whether the amount of a chemical substance taken up by the organism is harmful or not. For substances that can be absorbed through the skin, individual exposures can be determined only by biological monitoring. When using BAT values, the medical exclusion criteria defined by the “Berufsgenossenschaft” (Employers’ Liability Insurance Association) in the guidelines for occupational medical check-ups must be observed. BAT values are not suitable for the derivation, by means of fixed conversion factors, of biological threshold values for long-term non-occupational exposures such as from air pollution or contaminants in food.

Correlations between BAT and MAK Values

When a substance is inhaled under steady state conditions in controlled laboratory experiments, the relationship between the BAT and MAK values can be expressed in terms of pharmacokinetic functions. Under workplace conditions, however, it is not necessarily possible to deduce the level of a substance to which a particular person was exposed from its specific biological parameter in that person because a series of other factors in addition to the amount of substance in the air can determine the extent of exposure of the organism. These factors include the level of physical activity (respiratory minute volume), absorption through the skin and individual variations in metabolic or excretory patterns.

It is therefore particularly difficult to evaluate field studies which describe the relationships between internal and external exposure to substances which can be absorbed percutaneously. Experience has shown that studies of such substances frequently yield discrepant results. These discrepancies are attributed to different levels of dermal exposure under the different study conditions. When evaluating such results to determine relationships between MAK and BAT values, priority should be given to studies in which the data suggest that skin absorption played a minor role.

In general for substances with low vapour pressure which are readily absorbed through the skin, there is no correlation between exposure concentration and body burden. For these substances a BAT value can often be established only on the basis of a relationship between body burden and effect.

In addition, the concentrations of substances in the workplace air may vary with time and the biological parameters may not vary to the same extent. Therefore observance of BAT values does not make it unnecessary to monitor the concentrations of substances in the workplace air. This applies especially for local irritants and caustic substances. When evaluating macromolecular adducts of foreign substances it should be borne in mind that the persistence of these adducts can lead to discrepancies between the pattern of external exposure and the behaviour of the biological parameters. Similar considerations apply

for all highly cumulative substances such as heavy metals and polyhalogenated hydrocarbons.

In spite of all these interfering factors and the consequent differences in the definitions of MAK and BAT values, the two thresholds are generally based on equivalent effects of substances on the organism. However, for substances for which the MAK value is not established on the basis of systemic effects but because of local irritation of skin and mucous membranes, a BAT value can still be based on “critical toxicity” resulting from systemic exposure. In such exceptional cases where the MAK and BAT values are based on different end points, the two values do not necessarily correspond.

Surveillance

The protection of the health of the individual, which is the reason for establishing BAT values, can be monitored by periodic quantitative determination of the chemical compounds or their metabolites or of biological parameters in biological material. The methods used must be diagnostically specific and sensitive enough for the purpose, acceptable to the employee and practicable for the physician. The sampling time, that is, the measurement strategy, must take into account both the exposure conditions at the workplace and the pharmacokinetics of the substance. As a rule, especially for substances which accumulate in the organism, this may be achieved by taking samples at the end of a working day after an extended period of work (working week).

During exposure to gaseous substances which are metabolized rapidly and for which the blood air distribution coefficient is larger than 10, it must be taken into account that the concentrations of the substances in blood and tissues are positively correlated with the level of physical activity.

The concentrations of inhaled gaseous substances in blood and tissues of persons working under hyperbaric pressure have been shown to be correlated positively with the pressure. In such cases the observance of the BAT value must be monitored more frequently as the BAT value is attained in such workers at lower exposure concentrations than in persons working at normal pressures.

Whole blood, serum and urine samples are used as assay materials, occasionally and under certain conditions, also samples of alveolar air. Saliva and hair samples are not suitable assay materials for occupational medical biomonitoring.

The analytical methods must yield reliable results and meet the requirements of statistical quality control (TRGS 410 of the regulations for hazardous chemicals at the workplace). In the collection “Analysen in biologischem Material” (available in English in the series “Analyses of Hazardous Substances in Biological Materials”), the Commission’s “Analytical Chemistry” group has compiled a series of methods which may be considered reliable for this purpose.

Evaluation of Analytical Data

Like any results of laboratory investigations, toxicological analytical data can only be evaluated given knowledge of the whole situation. As well as the other medical findings, especially

- the dynamics of pathophysiological processes
 - the short-term effects of exposure-free periods
 - the long-term effects of ageing
 - the specific workplace conditions
 - intensive physical activity and unusual conditions of atmospheric pressure
- and any individual background exposures must be taken into account.

Results from analyses in biological material are subject to medical discretion. Only the physician who is responsible may interpret the results.

BAT values are established on the basis of the results of scientific studies and practical medical experience.

Allergenic Substances

Depending on individual disposition, allergic reactions can be induced by various kinds of substance, more or less rapidly and in differing degrees of severity after sensitization of, for example, the skin or respiratory passages. The observance of BAT values cannot provide a guarantee that such reactions will not occur.

Mixtures of Substances

BAT values apply as a rule for exposure to pure substances. They are not necessarily applicable for persons exposed to preparations containing more than one toxic substance (blends, mixtures, solutions). This is especially true for BAT values requiring determination of the substance itself or its metabolites. For mixtures of components with similar effects, a BAT value based on a biological parameter can be helpful in the assessment of health risks, as long as it provides a measure of critical clinical-functional effects of the components. The Commission makes every effort to define and publish such criteria for the biological effects of interfering components of mixtures.