

# Importance of sex-specific factors in the establishment of BAT values

## Assessment Values in Biological Material – Translation of the German version from 2000

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Biological tolerance values (BAT values) are to be established paying special attention to the rules of toxicokinetics. The question here is whether sex-specific differences between men and women can be found that would have to be accounted for in establishing BAT values.

This question has been dealt with in detail by Silvaggio and Mattison (1994), and can thus be referred to. Accordingly, anatomical and physiological parameters such as body weight and body surface are to be taken into account, as well as the various volumes of blood, organs and tissues, metabolic differences, and cardiovascular, pulmonary, gastrointestinal and renal structure and functional differences. These may affect internal exposure and the effects of chemical substances. As regards these parameters, there are already wide differences within a single sex and there is a marked overlap between the two sexes. Pregnancy must be accounted for as being a separate state.

In contrast to the experimentally well-established conditions in rats, where the males have a higher enzyme capacity in their oxidative metabolism of xenobiotics than females, the differences between men and women (apart from the state of pregnancy) as regards the metabolic activity of their xenobiotic-metabolizing enzymes can be neglected. Toxicokinetic differences between the sexes in humans arise from the fact that, compared with women, men have on average a higher body weight and consequently a greater body surface area; in addition, their body composition with regard to water balance is different. The proportions of total body water, extracellular water, whole blood, plasma and erythrocyte volumes are higher in men than in non-pregnant women. When, therefore, a dose of a water-soluble xenobiotic is taken up by the body, a higher distribution volume is found on average in men and thus a lower resulting concentration of the substance in their body fluids. This influences in turn the degradation rate of the xenobiotic.

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In the state of pregnancy, changes occur in body weight and plasma volume, extracellular fluid space, in total body water and body fat, and in plasma protein levels, which affect the distribution of xenobiotics. An initial body weight averaging 50 kg increases during pregnancy to about 63 kg in the 40<sup>th</sup> week. The total body water increases from 25 l to 33 l at the time of birth, although it still has a total which is lower than that in an average male (42 l). The extracellular fluid volume increases in the course of pregnancy from 11 l to 15 l, compared with 18.2 l for an average male. The plasma volume increases from 2.5 l to 3.8 l during pregnancy but is on average 3 l in males. This means that considerable variations in the toxicokinetics of xenobiotics can occur during pregnancy.

With regard to the establishment of limit values, the following points are of importance:

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 limited compared with the uncertainty involved in establishing limit 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 regulation it is the effects on the embryo and foetus which are of particular importance (see Section “Prenatal toxicity” in the MAK Value Documentations).

These considerations show that although differences between the sexes in the toxicokinetics and, due to that, in the level of internal exposure and effects produced by an external exposure can be named theoretically, the practical importance of these differences is nevertheless limited. This means that they need not, as a rule, be taken into account as regards the establishment of a limit value.

## 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](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.

## References

- Silvaggio T, Mattison DR (1994) Setting occupational health standards: Toxicokinetic differences among and between men and women. *J Occup Med* 36(8): 849–854