VCI Position Paper

Limit Values for Endocrine Disruptors

Endocrine active (hormone active) substances are substances that interact with the hormone system. Where these substances have a lasting harmful effect they are called endocrine disruptors (ED).

Ongoing discussion

Is it possible to determine thresholds and limit values for endocrine disruptors? This question has been discussed for some time among experts and in the political arena, focusing on the environment most recently. The answer to this question has fundamental impacts on the usage of chemicals.

Significance of the hormone system

Hormones are important messenger substances for the organism. Endogenous hormones are produced in glands, released into blood and transported to target organs, where they bind to receptors and thus unfold their effect. There are many hormone-driven reactions in the organism. Processes such as e. g. metabolism, growth and development can be controlled and regulated in this way. Beside endogenous hormones, there are further relevant substances: natural substances with hormonal effect (e. g. some plant ingredients) and hormone active synthetic chemicals.

What is a threshold?

A threshold is an intake (dose of a substance) or an exposure concentration above which harmful effects are observed. No (harmful) effects caused by a chemical substance are observed below the threshold. Population-relevant effects are examined for an environmental assessment.

Generally, the dose is decisive for the effect. For this reason, dose-effect relationships are examined in assessments of chemicals – this also applies for hormone active substances. This means that a substance is tested in various concentrations and according to generally recognised methods. In most cases, a threshold can be determined on this basis.

As there is an immense number of species, not all animal and plant species in the environment can be tested as to potential harmful effects. Therefore, substance properties are tested in proxy species. The thus determined threshold is the dose or concentration from which undesirable population-relevant effects can be observed. Below the threshold, no harmful effects are to be expected on the populations of a certain species. The threshold in the environment is the lowest value that was determined in the selected species. It is expressed as “no observed effect concentration” (NOEC) or a low “effect concentration” (ECx, e.g. EC10 or EC20).

What is a health-based limit value for humans?

The health-based limit value states the dose up to which a substance is safe for humans and no damage is to be expected. Limit values are important in assessments

of chemicals, in order to ensure their safe handling and use.

The limit value is obtained from the threshold. However, the limit value is always much lower, because additional safety factors are applied. Here, the precautionary principle is followed, with safety factors for particularly sensitive groups of persons (e.g. children, pregnant women) being taken into account when deriving limit values. Such factors also exist for the transfer of data from animal testing to humans and the type of studies used for deriving the limit values.

How are limit values derived for the environment?

The limit value for the environment is called “Predicted No-Effect Concentration (PNEC)”. It is derived from the lowest threshold determined in experiments. The PNEC, which is intended to ensure protection for all species, is laid down e.g. by resorting to safety factors. A safety factor wants to safeguard protection also for particularly sensitive species, as compared with the tested proxy species. The safety factor also takes into account possibly existing differences that have to be assumed because of the various types of studies used for deriving the limit values.

For which substances can no thresholds be derived?

No thresholds – and, consequently, no health-based limit values – can be laid down for substances where (theoretically) any exposure can cause damage. Examples are some carcinogenic substances which directly damage the DNA. They have irreversible effects, and no level can be stated up to which the substance is not harmful. A safe usage under adequate control is therefore not possible.

Testing according to international guidelines

The absence of effects can never be clearly proven scientifically. Given the large number of species in the environment, the absence of substance-induced disruptions of the hormone system cannot be proven beyond doubt for all species in their entirety, either. Against this backdrop, an instrument is needed to identify from the total of natural and synthetic substances those that really call for action due to their harmful effects.

A tiered and standardised test regime with proxy organisms should be followed for a reliable and comparable assessment of chemicals.

In order to give due consideration to the specific aspects of endocrine effects, certain standardised test methods (e.g. OECD Framework) have been developed or further developed alongside a number of screening tests. With the testing of organisms throughout their whole life cycles or over several generations, the standardised tests also enable proof of delayed effects and of potential effects at low concentrations.

Standardised test methods bring a high degree of reproducibility and reduce uncertainties regarding the effects that are really caused by substances.

Studies that were not conduced according to standardised test methods can be used as additional information, supplementing the data from guideline tests.

Reasons why thresholds can be derived for endocrine disruptors:

- Most hormonal influences do not cause any damage. Normally, the organism remains in balance also with measurable hormonal reactions - up to a certain threshold. The threshold can be low in certain development phases, but it can be determined with suitable methods. This enables the derivation of effect-based limit values in principle
- There are many hormone-driven reactions in the organism that bring time limited fluctuations of the hormone system. We influence the hormonal regulation of our bodies with e.g. consumption of caffeine. Forms of behaviour such as intensive sports can trigger hormonal effects too. However, these reactions have only temporary effects and do not cause permanent damage. Comparable reactions are known in the environment, even though the short-term fluctuations of hormone concentrations in environmental organisms are studied less intensively than those in humans
- The effect of a hormone active substance depends, inter alia, on how strongly it binds to the respective hormone receptor (affinity). Hormones unfold their effects according to the “lock-and-key principle”. A hormonal effect is triggered only if the hormone (ligand) fits like a key in the lock (“receptor”). Many hormone active chemicals bind only weakly, because they do not fit well into the “receptor look”. Another important point is which cellular reaction triggers the binding of a hormone or another ligand to the receptor.

THE VCI IS CALLING FOR THE FOLLOWING:

Derive limit values for endocrine disruptors

The dose or the exposure concentration are decisive for the effect of a substance. This applies also for endocrine disruptors. Therefore, limit values can be derived for these substances too. Sensitive species or the given data situation are taken into account in the form of safety factors.

There is no evidence of endocrine disruptors having to be assessed as “substances without threshold concentration” generally. This also holds true in respect of the environment.

Consider risk assessment in regulation

The safe handling and use of hormone active substances and endocrine disruptors is possible, relying on a sound risk assessment. Acceptance of derived limit values is an essential prerequisite for meaningful and risk-adequate regulation

Take into account the state of science

Endocrine disruptors and their effects can be assessed on a scientific basis. Further research is necessary in some fields for a better understanding of the effects of endocrine disruptors. The chemical industry is actively involved in these research efforts.

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