

## Questions and answers on endocrine disruptors

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Plasticisers in plastics, contaminants in bottled mineral water or natural constituents in plants, no matter whether naturally occurring or of artificial origin, compounds which are suspected of causing adverse effects on the endocrine system are currently in the focus of intense public debate. The Federal Institute for Risk Assessment has compiled questions and answers concerning these substances which are referred to as endocrine disruptors.

### What are endocrine disruptors?

Numerous body functions in humans and animals are controlled by messenger substances such as hormones. This system of hormones is perfectly balanced and, in conjunction with hormonopoeitic glands, it makes up what is called the endocrine system.

The term endocrine disruptors refers to substances that could have adverse health effects by disturbing the endocrine system once they would enter the body at an effective dose. Endocrine disruptors can occur naturally (phytohormones) or are being produced artificially (synthetic). Endocrine disruptors thus do not belong to a defined chemical category.

### How do endocrine disruptors take effect?

Endocrine disruptors can affect the endocrine system in different ways. Some of these substances may interact directly with hormone receptors thereby mimicking the effect of the physiological hormone or blocking the receptor binding site (agonistic and anagonistic effects respectively). In addition, some endocrine disruptors become effective at the level of expression of receptors or cofactors, the transduction of the hormone signaling within the cell, the metabolic turnover of hormones (e.g. inhibition of the enzyme aromatase), or the distribution of hormones in the body.

### Is the efficacy of individual endocrine disruptors known?

For endocrine disruptors which interact directly with a hormone receptor, it might be obvious to assume that endocrine activity and receptor affinity are correlated with each other. According to the current state of knowledge, however, the binding affinity of individual receptors alone does not provide sufficient information on the efficacy of a substance since kinetic factors are to be considered, too.

### Which natural substances can influence the endocrine system?

Certain secondary plant ingredients such as isoflavones from soy beans or clover are well known examples of naturally occurring endocrine disruptors and are therefore referred to as phytohormones. They can become effective by binding to one of the estrogen receptors. Similar to isoflavones, lignans may also exert estrogen-like effects. The most well-known source of lignans is linseed. Further phytohormones are flavones, flavanones, chalcones and coumestanes. Also, some phytopathogenic fungi produce substances with hormone-like activity and thus are being referred to as mycoestrogens (e.g. zearalenon).

### Which synthetic substances are suspected to affect the endocrine system?

In addition to synthetic hormones such as ethinylestradiol, which were for example used in medicinal products for birth control, there are other substances that have an unintentional adverse side-effect on the endocrine system. The most well-known synthetic compounds with potential endocrine effects include monomers in plastics such as bisphenol A, additives such as certain phthalate esters, and organotin compounds such as tributyltin (TBT). In addition, surfactants such as nonylphenol or brominated flame retardants such as polybromi-

nated diphenyl ethers (PBDEs) may affect the endocrine system. Similarly, dioxins or PCBs, which are spread throughout the environment, are known for their adverse effects on the endocrine system. Furthermore, some plant protection agents (pesticides) are also discussed as potential endocrine disruptors.

#### **How can endocrine disruptors enter the body?**

There are several pathways by which endocrine disruptors can enter the body including the digestive tract, lungs or skin. However, the primary focus is on the oral intake through food and drinking water. In these cases the foodstuffs themselves may contain hormone-like substances naturally such as phytoestrogens or they may have been contaminated with chemicals from the environment that affect the endocrine system. Furthermore, hormone-like substances can also migrate into foodstuffs from food contact materials, such as packaging, plastic dishes or drinking bottles and thus enter the body. For smaller children, there is an additional entry pathway through “mouthing” of toys made of plastics that contain plasticisers. However, the critical phthalate plasticisers have been banned from toys.

#### **Which health effects are being discussed?**

Public debate is currently focusing on substances that influence the sexual endocrine system (estrogen or androgenic hormones). These substances are suspected to stunt the development of children during pregnancy or during certain developmental phases such as puberty. Endocrine disruptors are also thought to potentially inhibit fertility and promote the development of certain tumors. Epidemiological studies have shown an increase in tumor rates in organs that are hormonally regulated such as breast and prostate cancer. The development of such tumors is aided by a number of factors such as overweight or alcohol consumption. Endocrine disruptors are under consideration as an additional potential risk factor. It is also debated whether or not endocrine disruptors are involved in the noted inhibited fertility of men as a result of undescended testicles or decreased sperm counts. However, to date no causal relationship has been scientifically established between the exposure to endocrine disruptors through foodstuffs or the environment and adverse health effects.

#### **How is consumer health risk in regard to endocrine disruptors being assessed?**

Exposure, that is the extent to which humans come into contact with endocrine disrupting substances, is a deciding factor in health risk assessment. Current data on exposure levels to individual substances such as bisphenol A or phthalates have not provided substantial scientific proof of a health hazard, not even for most susceptible groups of consumers such as small children and adolescents during puberty. Nonetheless, the overall exposure to endocrine disruptors should be reduced as much as possible.

#### **How are consumers protected from possible adverse health effects of endocrine disruptors?**

In order to protect consumers from adverse health effects of compounds suspected to exert endocrine activity, maximum levels are derived, for example, for food contact materials that define the maximum amounts which may be released from these into food. These levels are also referred to as migration limits. If these limits are adhered to, according to current knowledge no adverse health effects are to be expected.

For residues of plant protection products, the EU has defined maximum levels that may not be exceeded. As long as these are adhered to, consumers are expected to experience no adverse health effects. Potential endocrine disrupting properties are also taken into account when these maximum residue levels are determined.