Risk Assessment of Endocrine Active Compounds

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Highlights

- Chemicals that could potentially cause endocrine disruption (ED) are treated differently in regulation than other toxic substances
- Clear examples of ED have been established in some wildlife species (e.g. tributyltin-induced masculinization in snails), but still explicit links to declines in populations are rare.
- Associations between certain chemicals and human health effects have been made but a causative role of these chemicals in diseases and abnormalities possibly related to ED has not been verified.
- There are some relevant and potentially serious effects e.g. in the male reproductive tract, but we need to identify causal factors when implementing control of these substances, otherwise we may leave the problem unattended.
- In determining causality, special attention should be given to exceptional high exposures to endocrine disrupting chemicals (EDCs)
- Present regulatory toxicology test guidelines, in particular guidelines for ecotoxicity testing, cannot detect all endocrine disrupting effects. New guidelines have to be developed - with particular emphasis on in vivo data.

Summary

Karl-Heinz Florenz MEP welcomed some 40 delegates to the second AllChemE seminar at the European Parliament. Mr Florenz is heavily involved in Chemical Policy work in the parliament and was pleased to be hosting this discussion. Simon Webb on behalf of AllChemE, introduced AllChemE and our two speakers.

Prof. Peter Calow defined Endocrine Disrupters (ED) as substances that cause adverse health effects by altering the function of the endocrine system. EDs are treated differently than other toxic substances as they are suspected to act in the body at low concentration, which would mean that exposure to low concentrations over extended periods of time may cause adverse effects. Prof. Calow used the example of a widely publicised study on the effects of Atrazine (a herbicide) in feminisation of frogs to illustrate the uncertainties in demonstrating cause and effect in a complex and confounding real world. He demonstrated that from a scientific perspective, the case against Atrazine was ambiguous. He emphasised the need to treat all studies carefully and critically. Though some clear examples of ED effects from chemicals have been established in the wild, e.g. masculinization (imposex) by tributyl tin (TBT) in marine snails, the science is far from established in many other cases. In addition, laboratory work has not always translated into the same effects in nature. Prof Calow stressed that an effect in individuals might not translate into adverse effects in populations in the wild. In particular, he argued that using the precautionary principle to deal with this issue might be ill-advised, as lack of understanding of the actual issue could mean it would hinder rather than help the resolution of the problem.

Prof. Joseph Vos concentrated on the human health and mammalian effects of EDs.Health effects reported that have been associated with exposure to endocrine disrupting chemicals concern the male reproductive tract (decreased sperm quality, cryptorchidism, hypospadia, testicular cancer and prostate cancer) and breast cancer and endometriosis in women. In all these health disturbances, a causative role for these chemicals has not been not verified . Further evaluations of the human health effects which have been associated with endocrine disrupters are required to identify the underlying causes. In this, special attention needs to be given to exceptionally high chemical exposures and to the health consequences of phytoestrogens in human food.

Prof. Vos indicated that present regulatory toxicology test guidelines, in particular the guidelines for ecotoxicity testing, cannot detect all endocrine disrupting effects. Therefore, current test guidelines should be enhanced or new guidelines developed. There was a reliance on in vitro (test-tube) assays for predicting endocrine disrupter effects. This approach may generate false-negative as well as false-positive results. Therefore, more emphasis should be put on animal testing.

Prof Vos described a study of the Erasmus University on Dutch preschool children which has shown that perinatal background exposure to PCBs and dioxins might be associated with a greater susceptibility to infectious diseases in childhood. However, common infections acquired early in life may prevent the development of allergy, as exposure to bacteria appeared to be associated with a lower prevalence of allergic diseases (a finding in line with the so-called “hygiene hypothesis”). Prof. Vos presented his own semi-field study of European harbour seals where increased exposure to PCBs caused suppression of the immune system. This explains that seals were more susceptible to distemper epidemics that led to the massive mortality in seals in north-western Europe in 1988 (and again in 2002).

Prof. Vos concluded by discussing current work on brominated flame retardents such as polybrominated biphenyl ethers PBDEs which have been identified as potential EDs. Some, but not all, of these chemicals are bioaccumulative, and have been found in wildlife and humans. The EU-funded FIRE project (http://www.rivm.nl/fire) could answer the questions whether margins of safety for these chemicals are sufficient by systematic monitoring and generation of toxicity data.

Debate

An interesting debate followed, with questions on the role of modern analytical techniques on the development of this area, appropriate application of the precautionary principle and the confounding aspects of habitat and climate change in amphibians. Vigilance and sound science is important, stressed both Calow and Vos: in retrospect it is possible that the role of TBT in the marine environment could have been detected and acted on earlier as pertinent evidence was likely available.