What happens nowadays with the dose-effect relationship beyond the scientific community?

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During the last decades the rapid development of the analytical chemistry has become closely connected with the public perception of dose effect relationships. With respect to dose effect relationships and the way these are often communicated by NGOs, politicians and risk managers to the public it is fairly easy to select some recent toxicological 'bloopers'. This presentation will focus on some remarkable examples using dioxins, PCBs, brominated flame retardants, UV screens and container fumigants, including methylbromide. One the one hand examples will presented in which the public is clearly scared by NGO's using the fact that extremely low levels of chemicals are found in humans, from which it can hardly be expected to have any adverse health effects based on toxicological studies. On the other hand there is sometimes a remarkable reluctance of governments and politicians to address human exposure scenario's, in which there is at least from a toxicological point of view clear reason for further study to exclude possible adverse health effects.

For dioxins the differences between linear and non linear risk assessment approach used by the US versus the rest of the world is an illustrative example. At present the international scientific community after more than 25 years of research and billions of dollars or euros spend, most of it spend on analytical chemistry, still has not come to a consensus for risk assessment. Clearly this lack of consensus is bad for the international reputation of toxicologists and related scientist, especially considering the fact that dioxins are one of the best studied groups of compounds in the world.

A related topic is the risk assessment of dioxin and non dioxin like PCBs. If you look at the general dose effect relationships for both groups of compounds the toxic potency of non dioxin like PCBs compared with the dioxin like PCBs is four to six orders of magnitude less. We are talking about differences between no and lowest adverse effect levels between picograms and micrograms/kg/d for dioxin and non dioxin like PCBS, respectively. Presently dioxin like PCBs are adequately covered in the TEF concept for dioxin like compounds that is based on additivity and similar mechanism of action. Looking at the actual human exposure for both groups of PCBs the difference in the margin of safety that can be seen at background situation, is probably less than a factor 10 for dioxin like compounds but two to three orders of magnitude for the non dioxin like PCBs. As there is almost always a combined exposure to dioxins, dibenzofurans and PCBs at rather stable ratio's, one can question if it is really necessary to further spend research money on non dioxin like PCBs risk assessment from a point of dose effect relationship.

Another interesting topic is the brominated flame retardants, especially PBDEs. Three commercial mixtures are or have been on the market differing in the degree of bromination. The penta and octabromo PBDE mixtures have now been taken of the market as these congeners clearly bioaccumulate in the food chain. The technical decaBDE formulation is however still on the market as an effective flame retardant in a variety of products, like computers, TV's, electronics, clothes and household products. Although decaBDE is persistent and omnipresence in environment, it has a low bioavailability, does not bioaccumulate in the human food chain and is considered toxic only at very high (internal) dose levels. The case of decaBDE has now almost become a kind of religion and quite often opinions have nothing to do anymore with objective science. With respect to the risk assessment of decaBDE again there is a remarkable controversy between points of view of e.g. NGO's propagating a complete ban of production, while on the other side recent risk assessments of the JECFA and EU indicate no risk at the present background concentrations in humans.

Another interesting group of compounds with respect to risk assessment and dose effect relationships are the UV screens with estrogenic activity. In general, it can be concluded some common UV screens have an estrogenic potency that is 6 to 4 order less than that of endogenous estrogens. In spite of these low estrogenic potencies a number of properties of these compounds justify more attention from toxicologists and risk assessors. Quite a few are actually hydrophobic, accumulate in fish, and can be found in human milk and blood after application on the skin. Skin permeation can be as high as 35%, and some metabolites of these UV screens are 2-3 orders of a magnitude

more estrogenic than the parent compound. Although there are clear health benefits with respect to the use of UV screens, regulatory authorities and industry should not hide behind the apparent low estrogenic potency of the parent compounds without taken into account adequate (internal) exposure scenarios. It is therefore surprising that so few research initiatives have been undertaken during the last five years to establish the actual risk of these UV screens for sensitive groups e.g. those with history of estrogen dependent tumors versus their benefits to prevent skin cancer.

One of the most recent 'bloopers' in toxicology was the use of fumigants like methylbromide as fumigants in ship containers to kill insects. The Dutch National Health Institute (RIVM) did a good study on evaporation of these fumigants from a variety of household products and pharmaceuticals transported in these containers. It was shown that these neurotoxic fumigants were still evaporating from commonly used household products weeks or months after treatment at toxicological at least suspect concentrations. Furthermore, it was shown that methylbromide could also irreversible bind to high quality pharmaceutical products with unknown consequences for the composition and purity. Nevertheless no actions were taken by EU authorities when this information came available.

It is concluded that regulatory authorities, NGO's and industry nowadays handle dose effect relationships of toxicants sometimes in a rather sloppy way if it is politically or economically useful. In addition, the precautionary principle as advocated by NGO's has nothing to do anymore with dose effect relationships, but is presently more used to scare the public and gain new memberships, than it is based on sound science.