Is TEF outdated in the present form?

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Use of toxicity equivalency factors (TEF) of dioxin and dioxin-like compounds is a success story, which might have something to offer for other areas in toxicology and pharmacology[1]. The basis for the successful use of the concept is the reasonably well-understood mechanism of action based on a single AH receptor. It assumes similar efficacy for all compounds included in the concept. This prerequisite has not encountered major problems in the use of the concept so far. It assumes, and this is in fact the reason for its use, different potencies for different compounds. For practical purposes it is a huge advantage to be able to sum up the exposures into a single number in order to approximate the need for actions. This has been extensively used in the recent regulations on maximal concentrations of dioxin-like compounds by various authorities such as the European Commission. These maximal limits will incorporate dioxin-like PCB compounds in near future in addition to PCDD/Fs[2].

There is, however, another major problem in assessing the risks of mixtures of dioxin-like compounds than the potency. Environmental fate of different compounds is highly different. There are some examples according to which the spectrum of congeners may proceed fairly unchanged from one trophic level to the next. For instance, dioxin congener spectra of fishermen consuming high amounts of a specific fish, resemble the spectra in the fish to such an extent as to make it possible to predict the fish species consumed by a particular fisherman[3]. However, when comparing the spectrum of congeners in human beings (e.g. [4,5]) and in the most important sources [6,7] or in river[8] or sea bottom sediments[9], there are huge differences.

The problem arises when the same TEF concept is being used at different trophic levels, or even beyond this, for contaminated soils or sediments, and further for emissions. If congener spectra in human beings are totally different from those of emissions, some congeners obviously are carried through the chain of processes from a factory to population much more effectively than others. Then it is not reasonable to assess the risk of dioxins in contaminated sediment or factory smokestack by using similar equivalency factors. Then the equivalency factors obviously should be different for each medium, there should be internal human TEF, food TEF, air TEF, bottom sediment TEF, and exhaust gas TEF, possibly different for immediate sources such as traffic, and more distant sources such as industrial and waste incineration emissions. This would, however, make the whole concept unbearably complicated.

Especially in air pollution research one has been using increasingly a novel concept intake fraction (iF). It has been defined as a fraction of total emission that is, at a population level, inhaled or ingested by human beings[10, 11]. Typically it is in case of indoor air pollutants of the order of 10^{-4} to 10^{-2}, in the case of outdoor air pollutants from 10^{-5} to 10^{-4} for local emissions such as traffic, and from 10^{-6} to 10^{-5} for persistent transported compounds and 10^{-8} to 10^{-7} for reactive transported compounds. Intake fraction is by nature an arbitrary and very rough method of helping risk managers, but it is very robust, and adds a very easily understandable, comparable, and acceptable dimension to risk assessment.

How about using iF in dioxin risk assessment? The logical way of doing this would be to assess internal TEF for human being (or for wildlife for those who are interested in ecotoxicology). Then when assessing the risk of dioxins in any other media, this internal TEF should be multiplied by iF to give the matrix specific equivalent amount of the compound (MS-TEq) present as a quantity of A, and by bioavailability factor B to take care of varying absorption.

$$\text{MS-TEq} = iF \times B \times TEF \times A$$

The great advantage of dividing the internal effect and the intake to separate entities, is a logical and much simplified system. The TEF values and the iF and B values can be independently developed further by their own specialists (for examples of problems with iF, see [12]) without a need to try to embrace all factors involved into a single discussion, which seems to be impossible anyway. By knowing the concentrations in the population and the emissions of compounds, it is possible to estimate, by congener, the relative differences in their iFs.

If we now for the sole purpose of illustration assume that iF of 2,3,4,7,8-PeCDF is 10^{-5} and that of 1,2,3,4,6,7,8-HpCDF 10^{-7}, and B factors 0.6 and 0.4, resp., we can derive

2,3,4,7,8-PeCDF MS-TEq = $10^{-5} \times 0.6 \times 0.5 \times A = 3 \times 10^{-6} \times A$

and

1,2,3,4,6,7,8-HpCDF MS-TEq = $10^{-7} \times 0.4 \times 0.01 \times A = 4 \times 10^{-10} \times A$

The advantages for risk assessment of using MS-TEq instead of TEq are the greater the further off from the human being we assess the risk along the transportation route. Because e.g. 2,3,4,7,8-PeCDF seems to enter all the way to the human level more effectively than, say, hepta congeners, MS-TEq will emphasise the role of 2,3,4,7,8-PeCDF and downplay the role of heptas, not only because of their lower potency, but additionally because of their lower penetration of the food chain. The method may be rough and operating on average basis, but it is far better than using plain TEq values. Therefore it is worth developing further and to derive experimentally congener-specific iF values. Dioxins are an ideal group of chemicals to use this kind of approach for, because a short-term environmental exposure is not important, but integrated exposure over the years of many chemicals. This may be assumed to reduce the impact of inaccuracies of the method.

When TEF concept is further developed, we propose that the level of TEF would be explicitly determined to be the internal environment of human body. In this case TEF values are basically determined by two factors, relative potency and elimination kinetics. The basis of TEF would be the potency compared with that of TCDD as assessed by various toxicological methods. This value would be corrected upwards, if the compound would be eliminated more slowly than TCDD thus resulting with time in higher relative body burden than that of TCDD. The value would be corrected downwards, if the compound would be eliminated more rapidly than TCDD thus resulting with time in lower relative body burden than that of TCDD.

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