The use of TEFS for environmental risk assessment

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1. Introduction

The toxic equivalency concept has been developed as a tool for risk assessment of dioxin-like compounds during the last decades. In this concept individual halogenated compounds are each assigned a toxic equivalency factor (TEF) relative to a reference compound, usually 2,3,7,8-TCDD [1-3]. Dioxin-like compounds may cause a wide range of toxic and biochemical effects from which most of them are thought to be initially mediated by a single intracellular protein, the Ah-receptor [4]. Based on this mechanism of action additivity of these effects of individual compounds in a mixture is supposed. This prerequisite is supported by a wide range of results from both *in vivo* and *in vitro* experiments [5-9].

TEFs have now been determined for the most toxic chlorinated dioxins (PCDDs), dibenzofurans (PCDFs) and biphenyls (PCBs). Although there is clearly consistency in the data for individual congeners it should be pointed out, that TEFs always have been determined from a range of data into one single value [1-3]. This range of data originates from the fact that these TEF values have been found to be endpoint as well as species specific in spite of the common Ah-receptor mediated pathway [10]. In addition, other mechanisms which do not necessarily have to be strictly Ah-receptor mediated cannot be excluded, e.g. interactions with the estrogen receptor and effects on neurotoxicity or perinatal development [11-13].

The present TEF values have mostly been derived from *in vivo* studies, in which data from (semi)chronic experiments with mammals have given preference over those obtained from acute or *in vitro* studies. The TEF concept is mostly used in relation to the human risk assessment to determine the total TCDD equivalency in food items. When applied to other parts of the ecosystem generally similar TEFs are used as those applied for the human risk assessment. This in spite of the fact that relative toxicity of PCDDs, PCDFs and especially PCBs in birds and fish can significantly deviate from mammalian species [14-18]. In this paper the use of separate TEFs for PCDDs, PCDFs and dioxin-like PCBs for ecotoxicological risk assessment will be discussed.

2. Discussion

Available data. In the figures 1, 2 and 3 the reported TEFs for mammals, fish and birds are presented. TEF values are differentiated for these three groups of species and shown as ranges. Invariable, the information is more extensive for mammalian species than for fish and birds. A wide TEF range for a group of species does not necessarily implicate that extensive information is available. Such a range could very well consist of

two or three TEF values, which differ significantly.

In figure 1 the TEF values are presented for the most toxic PCDDs. Besides ranges of values for the three groups of species, the present NATO/CCMS I-TEF value is indicated with an asterisk [19]. From this figure it can be seen that 1,2,3,7,8-PnCDD appears to be slightly more toxic for fish and birds, more justifying a TEF value of 1 rather than the present 0.5. Data on 1,2,3,4,7,8,-, 1,2,3,6,7,8-, and 1,2,3,7,8,9-HxCDD are not very consistent, but appear to be in the same ranges as observed for mammalian TEFs. These data do not justify a suggestion for another TEF value for HxCDDs other than the value of 0.1. The present TEF value for 1,2,3,4,6,7,8-HpCDD is 0.01 and if this value is compared with those from fish and birds, it seems to be a clear overestimation as TEF values are almost two orders of an magnitude lower. A TEF value 0.001 or 0.0001 seems to be more appropriate. For OCDD no TEF values for fish and birds are presently available.

In figure 2 the TEF ranges for PCDFs are illustrated. Based on mammalian studies, the present TEF for 2,3,7,8-TCDF has been assigned 0.1. A single study done with fish indicated that the TEF was nearer to 1, while in contrast for birds the middle of the range was near to 0.01. For 1,2,3,7,8- and 2,3,4,7,8-PnCDF TEF values for fish and birds are in the same range as those reported for mammalian species. Based on these data a modification of the NATO/CCMS TEF values of 0.05 and 0.5 seems not justified. For 1,2,3,4,7,8-HxCDF with a present TEF value of 0.1, this value seems to be a slight over estimation and a TEF of 0.01 or 0.05 appears to be more appropriate for fish and birds. However, the limited data for 1,2,3,6,7,8-HxCDF indicate a TEF around 0.1 for fish and birds. As the present information for mammals, birds and fish on TEF values for the HxCDFs is very limited, an isomer specific differentiation seems not appropriate and the present value of 0.1 appears adequate.

In figure 3 TEF ranges are presented for *non* and *mono-ortho* PCBs, all exhibiting dioxin-like properties and abundantly present in the biotic environment. For these PCBs two set of TEF values have recently been suggested [2,3]. Which set of TEF values is more appropriate for risk assessment is clearly beyond the scope of this paper. For reasons of clarity only those TEF values for which a consensus was reached at a World Health Organization meeting in Bilthoven (The Netherlands), are indicated in figure 3 [3]. The suggested TEF for 3,3',4,4'-TCB (PCB #77) has been 0.0005, but as can be seen from the mammalian TEF range its value can vary two orders in magnitude depending on the endpoint and species involved. Data from bird studies indicate a TEF value of 0.01 when measured in systems using chicken embryos as a model. However, in various studies PCB #77 also showed to be non-responsive in (wild) bird species. In fish a TEF 0.0001 or 0.001 seems more appropriate. A similar pattern can be found for 3,3'4,4',5-PnCB (PCB 126) in which again mammals and birds have a similar TEF range, justifying the present value of 0.1. Again the TEF for fish is at least one order of a magnitude lower, suggesting a TEF between 0.001 and 0.1. For 3,3',4,4',5,5'-HxCB (PCB #169) only data for mammals and birds are available at this time and these are clearly in the same range and a deviation from the present TEF value of 0.01 is not justified. The consistent lower TEF value for fish appears also applicable for the *mono-ortho* PCBs included in figure 3. Both 2,3,3',4,4'- and 2,3',4,4',5-PnCB (PCBs #105 and #118) show for fish a TEF value which is at least one order of magnitude lower, than 0.0001 which have been presently assigned by the World Health Organization [3]. For 2,3,3',4,4',5-HxCB (PCB #156) no data on fish are presently available. Based on the data from PCBs #105 and #156 TEFs for birds and mammals appear to fall in the same range. However, PCB 118 shows a higher toxicity in birds than in mammals.

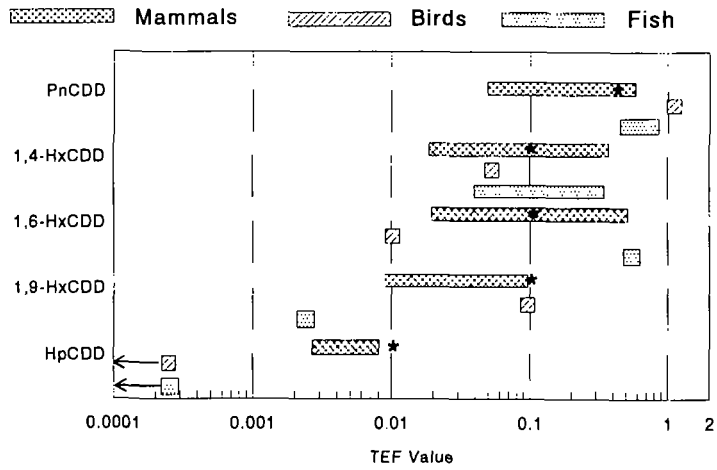

Figure 1. Ranges of Toxic Equivalency Factors in mammals, birds and fish for PCDDs.

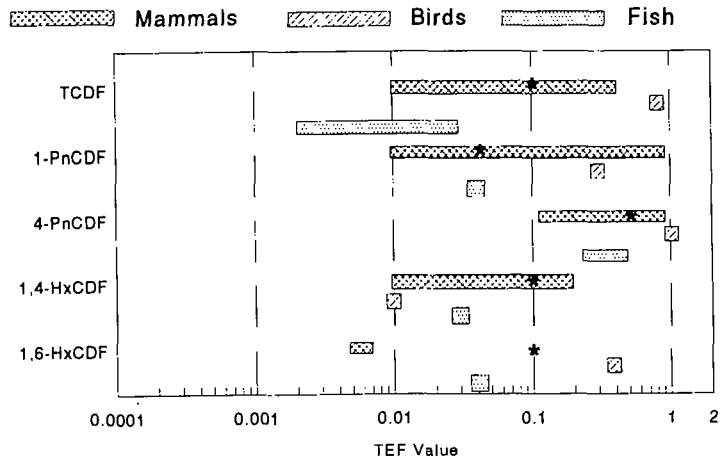

Figure 2. Ranges of Toxic Equivalency Factors in mammals, birds and fish for PCDFs.

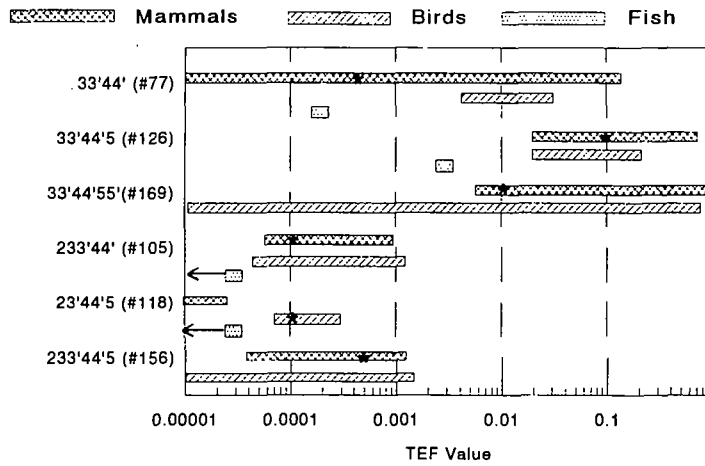

Figure 3. Ranges of Toxic Equivalency Factors in mammals, birds and fish for *non* and *mono-ortho* PCBs.

Implications for ecotoxicological risk assessment

Based on the scientific information presently available about relative toxicity of PCDDs, PCDFs and PCBs, it can be concluded that for ecotoxicological risk assessment separate TEFs (ECOTEFS) should be applied. Based on both evolutionary principles and observed congener specific potencies a division between mammals, birds and fish seems most feasible. From an ecotoxicological point of view it would also be preferable to include the group of invertebrates. However, to date no information about relative toxicity of these compounds is available for invertebrates. Nevertheless, it has been reported that some invertebrate species are highly sensitive for 2,3,7,8-TCDD toxicity [20]. For PCDDs and PCDFs the majority of the information indicates that mammalian TEFs are also applicable for birds and fish. Exceptions are found for 2,3,7,8-TCDF, 1,2,3,7,8-PnCDD and 1,2,3,4,6,7,8-HpCDD which have significantly higher or lower TEFs for birds and fish respectively, when compared with those from NATO/CCMS. The TEF values which are available for *non* and *mono-ortho* PCBs in fish invariable indicate that these values should be significantly lower than those for birds and mammals. These lower TEF values for fish could have significant implications for the risk assessment in the aquatic ecosystem. In contrast to human risk assessment, the species to species extrapolation might cause a much higher uncertainty in ecotoxicological risk assessment due to the large variety of species present. Clearly relative potencies can not be tested in all species to derive species specific TEFS and therefore a conservative approach would be recommended. In practice this could mean that the upper limit of a TEF range should be used for ecotoxicological risk assessment. In the future these ECOTEFs should be used in combination with no-observed or lowest observed adverse effect levels or concentrations (NOAEL(C)s or LOAEL(C)s), which at least should be differentiated for

mammals, birds and fish if the individual species sensitivity is not known. In this process it would be preferable if other endpoints than carcinogenicity, e.g. reproduction or perinatal development, should be included.

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