HUMAN AND MAMMALIAN TOXIC EQUIVALENCY FACTORS FOR DIOXINS AND DIOXIN-LIKE COMPOUNDS: THE WHO 2005 RE-EVALUATION*

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Introduction

An WHO-IPCS expert meeting was held in June 2005 (Geneva, Switserland) during which a re-evaluation took place of the toxic equivalency factors (TEFs) for dioxin like compounds, including some polychlorinated biphenyls (PCBs). The basis for this re-evaluation was a recently published TEF database by Haws and coworkers[1].

Results and Discussion

Evaluation of earlier and existing WHO-TEF values[2,3] and decisions about new values were based on a combination of unweighted relative effect potency (REP) distributions, expert judgement and point estimates. It was decided to use half order of magnitude increments on a logarithmic scale of 0.03, 0.1, 0.3 etc. for this re-evaluation. Changes in TEF values were decided by the expert panel for 2,3,4,7,8-pentachlorodibenzofuran (PnCDF), octachlorodibenzo-p-dioxin (OCDD) and octachlorodibenzofuran (OCDF), and one single value for all relevant mono-*ortho* substituted PCBs. Based on the new 2005 WHO TEF values it was concluded that the proposed changes have a limited impact on the total TEQ with an overall decrease in TEQ ranging between 10 and 25% for most food matrices relevant for human uptake.

The contents of this paper reflect the opinions and views of the authors and do not necessarily represent the official views or policies of NIEHS, NIH, USEPA or WHO.

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An important prerequisite of the TEF concept is additivity and the WHO panel recognized that this was further confirmed by recent *in vivo* mixture studies[4-7]. These mixture toxicity studies predicted WHO 1998 TEF values within a factor two or less and this accuracy is almost surprising as these TEFs are considered estimates with an order of magnitude uncertainty.

The expert panel also recognized that new studies provide evidence that non dioxin-like AhR agonists/antagonists can impact the overall toxic potency of 2,3,7,8-TCDD and related compounds. This possible effect on TEQs needs to be investigated further, but it was also concluded that it does not influence determination of individual relative potencies (REPs) or TEF values derived from experimental studies with individual congeners.

Several (groups of) compounds were identified that could be included in the TEF/TEQ concept in the future. Based on mechanistic considerations these include 3,4,4'-PCB (PCB 37), polybrominated dibenzo-*p*-dioxins (PBDDs) and dibenzofurans (PBDFs), mixed polyhalogenated dibenzobenzo-*p*-dioxins and dibenzofurans, polyhalogenated naphthalenes and polybrominated biphenyls (PBBs). However, for these compounds there is a clear lack of human exposure data and preliminary exposure assessments are recommended to indicate their relevance for humans with respect to TEQ dietary intake. Hexachlorobenzene might also be a possible candidate for inclusion in the TEF/TEQ concept, but only if it is unequivocally shown that impurities have not been the cause of earlier dioxin-like effects observed earlier. For polybrominated diphenylethers (PBDEs) it was concluded that there is no reason for their inclusion in the TEF/TEQ concept.

The WHO panel expressed concern about the application of the TEF/TEQ approach to abiotic environmental matrices such as soil, sediment, etc. as these values and associated methodology is primarily meant for estimating exposure via dietary intake. This type of application in abiotic environmental matrices has limited toxicological relevance and use for risk assessment, unless congener specific aspects like reduced bioavailability, environmental fate and transport of the various dioxin-like compounds are taken into account, because these properties may vary widely between congeners.

A number of future approaches to determine alternative or additional TEFs were also identified. These included the use of a probabilistic methodology to determine TEFs that better describe the associated levels of uncertainty and 'systemic' TEFs for blood and adipose tissue and total Toxic equivalency (TEQ) for body burden.

Literature

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