ACCOUNTING FOR TEF UNCERTAINTY IN DIOXIN EXPOSURE ASSESSMENTS

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Introduction

Polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans (PCDD/Fs, known as dioxins), and Polychlorinated biphenyls (PCBs) constitute a group of environmental and food contaminants. Their lipophilicity and chemical stability results in their occurrence in foods rich in animal and marine fat, the consumption of which is the major source of human exposure [1]. Toxic responses to these compounds include dermal toxicity, immuno-toxicity, endocrine toxicity and reproductive deficits for example, and as such, these compounds are of major concern to both human health and environment agencies. Dioxins and dioxin-like PCBs in food occur as mixtures of a number of different individual chemicals (known as congeners), which have different degrees of dioxin-like toxicity. Each individual congener is assigned a weighting factor (referred to as a Toxic Equivalency Factor – TEF) that reflects its toxicity relative to that of the most toxic dioxin – 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) [2]. The ensemble toxicity of a mixture is expressed in Toxic Equivalents (TEQ), that is the sum of the products of the concentration of each PCDD, PCDF and PCB with its respective TEF [3].

The World Health Organisation (WHO) has recommended a tolerable daily intake (TDI) of 1-4 pg WHO-TEQ/kg bw/day [4]. JECFA, the EU and other authorities have recommended intakes which are all close to this range. Current approaches to risk assessment for dioxins utilise the concept of TEFs. However, published TEFs are fixed values[2], but relative toxicity is both variable and uncertain. The term TEF "indicates approximately one-half to one order of magnitude estimate of the toxic potency of a compound relative to TCDD" [1]. In reality the uncertainty is probably larger than one order of magnitude, as indicated by the spread of results from individual toxicity studies for PCB 77 (Figure 1) [3].

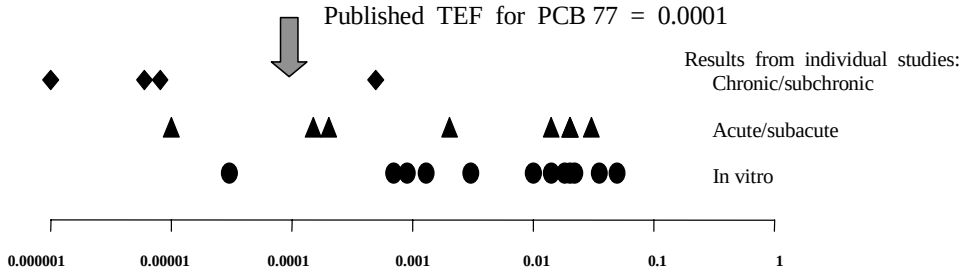

Figure 1. Comparison between standard TEF and experimental values for PCB 77 from individual toxicity studies.

Ahlborg *et al* [3] state that their TEFs "were based on studies with repeat dosing *in vivo* when available". For PCB 77, the TEFs from sub-chronic and chronic studies ranged from 0.000001 to about 0.0005, i.e. two and a half orders of magnitude. The range for PCB 126 is two orders of magnitude, and for PCB 156 it is 4 orders of magnitude. The upper ends of these ranges are 3x to 8x above the current nominal TEFs for these 3 PCBs.

Clearly, the implications of describing TEFs as point values are far-reaching in that the full range of exposures will not be captured in a risk assessment. Extreme consumers or sensitive individuals for example, may not be provided with sufficient protective measures. A more complete description for TEFs is therefore required that identifies the state of our knowledge, that is, our uncertainty regarding the *true* value for the TEF. This paper extends our previous work focussing in detail on TEF uncertainty and assessing in relation to an improved analysis[5,6].

Dietary Exposure

In this section we outline a model that compares the dietary exposure of an average UK consumer with and without uncertainty in the TEF. We show that significant departures occur in the exposure estimates in comparison with the upper WHO TDI of 4 pg WHO-TEQ/kg bw/day. Estimation of dietary exposure is affected by a number of uncertainties, including analytical measurement of dioxin and PCB concentrations, TEF values and estimates of food consumption. Additionally, the occurrence of "non-detects", where the concentration of a congener falls below the nominal limit of detection for the analysis, and the high cost of dioxin/PCB congener analysis limiting the number of samples analysed, resulting in significant sampling uncertainty introduce further uncertainties. All of these factors and comparability issues[7] must be considered carefully during an exposure assessment in order to interpret the results correctly. We addressed changes in dietary exposure caused by increasing the number of salmon portions consumed per week. Data were available from twelve samples of salmon representative of UK retail sale that were obtained around January 1996 and analysed for selected PCDDs, PCDFs and PCBs, reported as ng/kg or μg/kg fat. Fat content was measured for each salmon sample and used to convert the congener concentration to ng/kg or μg/kg salmon muscle. The total daily dietary exposure DD (pg TEQ/kg of bw/day) was determined by including the following factors; concentration of dioxins in the salmon consumed, the salmon intake rate, the concentration of dioxins present in other dietary components, and intake rates of dietary components excluding salmon. The concentration of dioxins in the salmon was then estimated for each salmon sample by combining congener concentrations and the corresponding TEFs.

We chose to represent the uncertainty around the TEF for each compound by a triangular distribution with the best estimate at the nominal TEF value, the minimum half an order of magnitude below, and the maximum half an order of magnitude above. For example, a TEF value of 0.01, would have a triangular distribution from 0.005 to 0.05, with the peak at 0.01. TCDD was not given any uncertainty since this is the reference congener to which all other TEFs are scaled. Where no uncertainty in the TEF was assumed we simply used the nominal reference value.

A one-dimensional Monte Carlo risk assessment was constructed using Crystal Ball® software running in Microsoft Excel® to explore the uncertainty surrounding total dietary exposure given uncertainty in parameters and concentration of dioxins observed in the samples of salmon and other food-types. Probabilistic descriptions were determined for these parameters and variables

based upon empirical data and level of sampling. The simulations were conducted using Latin Hypercube sampling and sensitivity analyses were performed using Crystal Ball® algorithms.

Non-detect cases were given distributions of uncertainty based on detected levels[6]. The sampling uncertainty associated with the mean salmon TEQ was also included, given the relatively small sample size. Finally, the uncertainties associated with the consumption of selected food-types were included, this enabled representation of the uncertainty in the actual average consumption[5]. Measurement uncertainty for each concentration was calculated retrospectively using a 'top down' approach as described in the Eurachem Guide[8]. This combines different sources of uncertainty that exist in the measurement process. These sources are, uncertainty due to variation and bias due to uncertainty about the true concentration of the certified reference sample.

Results and Discussion

To determine the background level of exposure to dioxins, the model was run without TEF uncertainty and with zero salmon consumed. The average exposure value was 1.47 pg WHO-TEQ/kg bw/day, with a range from 1.31 to 1.61 (Table I), this is in agreement with the findings of Smith *et al*[5]. The highest concentration of congeners in all samples was PCB 126, followed by 23478PeCDF or PCB 118. However, the relative contributions to uncertainty in the overall WHO-TEQ need not follow this order, since it also depends upon the uncertainty in the TEF and the measurement of the congener.

Table I shows the results for the exposure model with and without uncertainty in the TEF values. When the TEF values are fixed, as the number of salmon portions consumed per week increases, the total dietary intake increases as expected and there is a slight increase in the coefficient of variation of the distribution for exposure. Measurement uncertainty for non-*ortho* PCB 126 has more influence than other congeners, accounting for 60% of the total variance. Sampling uncertainty accounted for approximately 29% of the total variance.

Table I. Total dietary exposure pg TEQ/kg bw/day, including uncertainty in the TEF values.

	Salmon portions	mean	min	max	stdev	% above 4pg	CV
TEF fixed	0	1.47	1.31	1.61	0.046	0	3.129
Tef uncertain	0	2.91	1.9	4.30	0.37	0.25	12.715
TEF fixed	1	2.26	1.99	2.63	0.088	0	3.894
Tef uncertain	1	4.46	2.53	7.07	0.63	74.5	14.126
TEF fixed	2	3.05	2.58	3.84	0.16	0	5.246
Tef uncertain	2	6.00	3.78	10.3	1.11	99.4	18.5
TEF fixed	3	3.85	3.06	4.95	0.24	25.1	6.234
Tef uncertain	3	7.54	4.39	13.18	1.61	100	21.353
TEF fixed	4	4.64	3.38	6.08	0.31	98.6	6.681
Tef uncertain	4	9.09	4.67	17.16	2.17	100	23.872

When uncertainties in the TEF values were included; the mean daily intake of dioxins in the background diet was 2.91 pg TEQ/kg bw/day, with a range from 1.9 to 4.3 (0.25% of the

distribution is above 4.0). As more salmon portions are consumed, the daily intake increased and the degree of uncertainty associated with the estimated TEQ intake also increased. The consumption of a single portion of salmon each week elevated the daily intake to 4.46 pg TEQ/kg bw/day with 74% of the distribution above the upper WHO TDI of 4.0. Not only were the overall uncertainty (SD and range) greatly increased when the uncertainty of the TEF was included, but the average values increased also. The main contribution to the variance was the uncertainty in the TEF value associated with PCB 126 (68%), while measurement uncertainty of PCB 126 became the next most important contributor (22%): Table II.

Our results indicate that our understanding of risk from dietary exposure to dioxins and PCBs could best be advanced by improved characterisation of their toxicity. The data of Figure 1 suggest that the triangular distributions used in this study may actually underestimate the full range of uncertainty concerning the TEFs. As a first step we recommend that the existing toxicity data should be re-examined, to determine more objective estimates of the uncertainty surrounding the TEFs. In the case of salmon, our results indicate priority should be given to refining the TEF for PCB 126, but for other food types other congeners may be more critical.

Table II. A typical sensitivity analysis output showing the most significant contributors to the variance of the total dietary intake of dioxins in salmon. Entries indicate uncertainty in the TEF values or measurement uncertainty.

Source of uncertainty	Contribution to the variance %
PCB IUPAC 126 TEF	68.34
PCB 126	21.67
PCB IUPAC 118 TEF	0.97
12378 PeCDD TEF	0.83
PCB 118	0.81

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