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DIETARY EXPOSURE TO DIOXINS AND PCBs INCLUDING MEASUREMENT UNCERTAINTY AND LIMITS OF DETECTION

Mel Holmes, Andy Hart, Graham C Smith, Martin Rose, Roy Macarthur and Shaun White

Defra Central Science Laboratory, Sand Hutton, YORK YO41 1LZ United Kingdom

Introduction

Polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans (PCDD/Fs, known as dioxins), and Polychlorinated biphenyls (PCBs) are widely recognised as persistent environmental and food contaminants. Their lipophilicity results in their occurrence in foods rich in animal and marine fat, the consumption of which is the major source of human exposure [1]. 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 [2]. The overall toxicity of a mixture is expressed in Toxic Equivalents (TEQ), where the concentration or dose of each PCDD, PCDF and PCB is multiplied by its respective TEF and then summed [3]. The World Health Organisation (WHO) has recommended a tolerable daily intake (TDI) of 1-4 pg WHO-TEQ/kg bodyweight/day[4]. 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. Also, uncertainties arise due to the occurrence of "non-detects", where the concentration of a congener falls below the nominal limit of detection for the analysis. In addition, the high cost of dioxin/PCB congener analysis limits the number of samples analysed, resulting in significant sampling uncertainty. All of these factors and comparability issues[5] must be considered carefully during an exposure assessment in order to interpret the results correctly. This paper extends our earlier work [6] to explore in more detail measurement uncertainty.

Methods

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 ug/kg fat. Fat content was measured for each salmon sample and used to convert the congener concentration to ng/kg or ug/kg salmon muscle. The total daily dietary exposure DD (pg TEQ/kg of bw/day) was determined by using the following equation;

$$DD = \frac{CS \cdot SI + \sum CR_i \cdot RI_i}{BW}.$$

Where

CS – Concentration of dioxins in the salmon consumed (pg TEQ / kg).

SI – Salmon intake rate (kg /day), related to the total salmon portions consumed per week.

CR_i – Concentration of dioxins present in other dietary components (pg TEQ / kg).

RI_i – Intake rates of dietary components excluding salmon (kg /day).

BW - Bodyweight (kg). Average 70 kg individual used.

CS was then estimated for each salmon sample by combining congener concentrations and the corresponding TEFs. CR was calculated using literature sources to determine the average consumption of dietary components together with the associated WHO-TEQ per item. The total consumption of meat and fish products were adjusted so that as the number of salmon portions consumed per week increased, the corresponding amount of meat and white fish products decreased proportionately by an equivalent total amount[6].

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. The measurement of the concentration of the dioxins present in the salmon samples were given distributions of uncertainty based on detected levels and distributions were assigned to non-detect cases as described below. TEFs were assigned nominal values as recommended by WHO[4], although we investigated both point and probabilistic descriptions [7].

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 [6]. The software algorithm repeatedly selected an exact value at random for each uncertain parameter to calculate the mean total dietary exposure in pg WHO-TEQ/kg bw/day. The amount of salmon in the diet was varied explicitly from 0 to 4 portions per week in separate model runs, to assess the relative effect on dietary exposure. The 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;
1. Uncertainty due to variation, representing the variation of measurements of the same sample within our laboratory. This is estimated from replicate measurements of certified reference samples. This was sampled per once iteration for every congener/salmon sample.
2. Bias due to uncertainty about the true concentration of the certified reference sample that is supplied with the reference sample, this is based on variation between measurements made at a number of laboratories. This was sampled once per iteration for each congener.

The frequency of non-detects in samples and limits of detection during analytical measurements can differ significantly from laboratory to laboratory[5] giving the impression differences in totals exist when in fact, the source is the detection limit or protocol. We assumed that the values for the non-detect samples follow the same distribution as the detected values. These were generally approximately lognormal $P>0.05$. This is in contrast with our previous study where uniform distributions from zero to the limit of detection were assigned [6]. We therefore took natural logs of the detected values to estimate distributions for the standard deviation and mean using classical formulas, these express the uncertainties in the parameters. Samples taken from a normal distribution whose mean and standard deviation are also sampled values from the parameter distributions have logistic form. This defines the variation of the LOD and was subsequently censored at the limit of detection for each sample in question. This truncated distribution then

addresses the uncertainty in the measurement given a limit of detection and the fact we have limited samples with which to base our estimate.

The mean WHO-TEQ concentration found in salmon is taken as an estimate of the average to which individual consumers are exposed over a long time interval, although in fact it is likely that concentrations have since reduced. Since the true mean and standard deviation are unknown, and that the sample size is small (i.e. less than 30), the resulting sampling uncertainty is represented using Student's-t distribution.

Sensitivity analysis was performed using Crystal Ball® algorithms to determine the contribution to the variance due to sampling and measurement uncertainties. However, since forecasts were dependent upon several layers of assumptions, the analysis had to be calculated as follows. All dietary assumptions were frozen to enable the analysis of only measurement and sampling assumptions. The coefficients of variation (CV) of the simulated TEQ with and without sampling were calculated, the ratio providing the contribution due to sampling. All contributors to the variance without sampling were then reduced in proportion to determine the contribution of each of the measurement assumptions [6].

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). 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 measurement of the congener and LODs.

Table I shows results for the exposure model when uncertainty in the TEF values was ignored. 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. The variance of the estimated dietary intake can be partitioned into two main components: sampling uncertainty, and the measurement uncertainty for each congener (the latter combining bias in the reference value with uncertainty due to variation summed over the 12 salmon samples). 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 II. In contrast to our earlier study [6], measurement uncertainty in the congeners is the most influential component, this is because the same bias applies to all 12 samples, and as such, impacts across all samples.

This study indicates that both sampling and measurement uncertainty can have equal importance. Sampling uncertainty will dominate when we have a small number of samples i.e. less than 10, and so may be reduced by simply increasing the number of samples obtained. The most obvious way to reduce measurement uncertainty requires the uncertainty bounds of certified reference materials to be reduced. This may be achieved by increasing the number of laboratories taking part in the certification exercise and, the number of measurements made.

Finally, it is important to be aware of the assumptions built into this analysis, and the degree of caution required over the interpretation. We modelled a hypothetical average UK consumer as a

simplification in order to examine the effects of different levels of salmon consumption. For use in estimation of intakes, sampling should be designed to take account of many factors, the proportion of each food that is imported, variation in the countries of origin, seasonal and regional variation for example could play a pivotal role. If the exposure of sensitive sub-populations were the subject, then attention should also be paid to variation between consumers. This would require a substantially more complex model including distributions for individual consumption of each food type.

Table I. Total dietary exposure pg TEQ/kg bw/day, ignoring uncertainty in the TEF values. The distribution of risk as the consumption of salmon increases, in terms of daily consumption of dioxins per kg bodyweight. The Table shows the mean, range, standard deviation and percentage of distribution that would exceed the TDI of 4 pg.

Salmon portions	mean	min	max	st dev	% above 4pg	CV
0	1.47	1.31	1.61	0.046	0	3.129
1	2.26	1.99	2.63	0.088	0	3.894
2	3.05	2.58	3.84	0.16	0	5.246
3	3.85	3.06	4.95	0.24	25.1	6.234
4	4.64	3.38	6.08	0.31	98.6	6.681

Table II. Most significant contributors to the variance of the total dietary intake of dioxins in salmon. The percentage variation in the congeners relates to measurement uncertainty for each congener and not variation in congener concentration.

Source	Contribution to the variance %
PCB 126	60.36
Sampling	29.39
PCB 77	4.69
23478 PeCDF	1.45

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