UNCERTAINTY AND RECOMMENDATIONS

CONTAM Opinion on dioxins and DL-PCBs in food and feed

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Uncertainty Analysis

The CONTAM Panel performed the evaluation of the inherent uncertainties in the assessment of exposure to PCDD/Fs and DL-PCBs:

- following the EFSA **Guidance of the Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment** (EFSA, 2007)

- considering the WHO/IPCS report on '**Characterizing and Communicating Uncertainty in Exposure Assessment**' (WHO/IPCS, 2008)

Furthermore, uncertainties were reflected in

- Hazard identification and characterization
- Dose-response assessment and HBGV derivation
- Risk characterization

Summary of Uncertainty Analysis - EXPOSURE

Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of exposure of PCDD/Fs and DL-PCBs in food

Sources of uncertainty	Direction
Extrapolation of the occurrence data to the whole of Europe	+/-
Consumption data: different methodologies / representativeness / underreporting / misreporting / no portion size standard	+/-
Use of data from food consumption surveys covering only a few days to estimate high percentiles (95th) long-term (chronic) exposure	+
Occurrence samples not sufficiently described (e.g. classified only at the 1st level of FoodEx) were excluded	+/-
Imputation of missing fat percentages of certain foods in the Comprehensive Database	+/-
Effect of cooking/processing not taken into account	+/-
Contribution of other persistent AHR agonists	-

+ = uncertainty with potential to cause over-estimation of exposure/risk
- = uncertainty with potential to cause under-estimation of exposure/risk

Summary of Uncertainty Analysis – HAZARD ID/HC

Sources of uncertainty	Direction
Uncertainty in the relative potency of PCB-126	+
Uncertainties in WHO_{2005}-TEFs being rounded figures based on a wide range of relative potencies in animal and cell based studies	+/-
Epidemiological studies	
Uncertainty about systemic TEFs	+/-
Lack of measurements on PCDD/Fs and DL-PCBs other than TCDD	+
Non differential misclassification of exposure	-
True exposure being higher or lower than the estimate of exposure	+/-
True outcome is more or less prevalent than the estimate of the outcome	+/-
Confounding by other factors	+/-
Low number of epidemiological studies on the critical endpoint at low exposure	+/-
Critical study	
Co-exposure to other compounds which may impair semen quality	+
Uncertainty regarding critical window for effect on semen quality outcome	+/-

Summary of Uncertainty Analysis – HAZARD ID/HC

Toxicokinetic modelling

- Existing kinetic models not suitable to take into account variations in levels of PCDD/Fs and DL-PCBs during pregnancy and lactation
  - Milk intake of 800 mL per day applied throughout breastfeeding period
  - May result in overestimation of child exposure and a more conservative TWI (but rounded TWI robust for these effects)

- Body fat content was kept constant for infants and children
  - Known to be low at birth but rapidly increasing
  - initial serum level at birth underestimated
  - peak serum levels and subsequent decrease less affected
  - may affect relative amount stored initially in the liver

Summary of Uncertainty Analysis – HAZARD ID/HC

Toxicokinetic modelling

- Variations in body weight and fraction of body fat in mothers not taken into account by the modelling
  - may affect exposure and serum levels infants (both directions)
- Models developed for TCDD
  - less accurate for other relevant PCDD/Fs and DL-PCBs
  - the half-lives of PeCDD and 2,3,4,7,8-PeCDF are longer than for TCDD, those for other shorter
- The models are likely to underestimate the serum levels for these compounds but overestimate that for other congeners
  - Decided not to apply another uncertainty factor

Conclusion of the Uncertainty Analysis

The CONTAM Panel considered that:

- the impact of the uncertainties on the risk assessment of **PCDD/Fs in food** is **moderate**
- the impact of the uncertainties in the risk assessment for the **sum of PCDD/F and DL-PCBs in food** is **high**, due to the uncertainty in the relative potency of PCB-126 in humans

Overall, the assessment is likely to be **conservative**

Recommendations (I)

In order to improve the risk assessment for both humans and animals and reduce the uncertainties, the CONTAM Panel recommends that:

- The current WHO_{2005}-TEFs should be re-evaluated in order to take into account new *in vivo* and *in vitro* data. In particular, more insight into the relative potency of PCB-126 in humans is required
- There is a specific need to derive systemic TEFs for PCDD/Fs and DL-PCBs for use in epidemiological studies, also taking into account the results from human cells
- There should be an evaluation of the relative exposure contribution of other persistent chemicals, acting as agonists on the AHR, taking into account their toxic potencies
- To evaluate the applicability of the TEQ-principle, more research and understanding is needed on reported congener-specific effects of PCDD/Fs and DL-PCBs, including their relevance at low doses

Recommendations (II)

- Further improvement of toxicokinetics models is needed, including parameters dealing with pregnancy, breastfeeding and occasional exposure to high levels. Inclusion of PCDD/Fs, other than TCDD, and DL-PCBs is required. The use of in vitro models for further refinement should be considered

- Data from both experimental animal and epidemiological studies should be reported in a way that allows a better dose-response evaluation in order to improve the risk assessment. There is a need to develop a consensus methodology for data sharing between individual researchers and public health authorities

- There is a need for prospective developmental epidemiological studies on PCDD/Fs and DL-PCBs at low to moderate doses on, in particular, male reproductive outcomes and effects on the thyroid system. Follow-up studies on existing and previous cohorts with good information on pre- and postnatal exposure should be considered

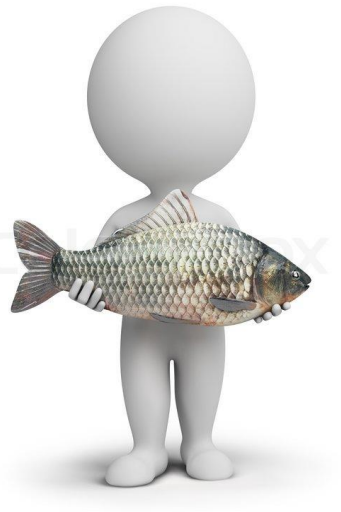
Recommendations (III)

- Validated and cost-effective methods are needed to assess exposure in small amounts/volumes of biological samples of animals and humans
- To better understand the adverse effects of PCDD/Fs and DL-PCBs, more insight is needed into the mode of action, especially in relation to observed critical effects
- Mechanistic studies on transgenerational (third generation) effects are needed
- To improve human exposure estimation, more occurrence data are needed on food of plant origin, especially where individual results of certain foods indicate potential higher contamination
- More data are needed on feed, provided by a greater number of European countries

Recommendations (IV)

- There is a need for an updated benefit-risk assessment of fish consumption that takes exposure to PCDD/Fs and DL-PCBs into account

Noting that,



The EFSA Scientific Committee in its statement on the benefits of fish/seafood consumption of methylmercury recommended that:

each country needs to consider its own pattern of fish consumption; especially the species of fish consumed,

and carefully assess the risk of exceeding the HBGV while obtaining the health benefits from consumption of fish/seafood.

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