TOX/2018/42

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Discussion paper on the EFSA Opinion on “Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food.”

Introduction

1. The European Food Safety Authority’s Panel on Contaminants in the Food Chain (CONTAM) were asked for a scientific opinion on the risks for animal and human health related to the presence of dioxins and DL-PCBs in feed and food.

2. The term ‘dioxins’ refers to both polychlorinated dibenzo-p- dioxins and dibenzofurans (PCDD/Fs).

3. Following a review of available animal and epidemiological data it was decided that the human risk assessment would be based on effects observed in humans and the animal data to be used as supportive evidence.

4. The CONTAM Panel has established a Tolerable Weekly Intake (TWI) of 2 pg TEQ/kg bw/week.

5. This paper provides a summary of the approach used by the CONTAM Panel to establish the TWI and a brief summary of the risk characterisation, in order for the Members to discuss and submit their comments.

Background

Previous Evaluations

6. Dioxins have been subject to a number of evaluations. The World Health Organisation addressed the safety of dioxins in 1990 where Tolerable Daily Intake (TDI) of 10pg TEQ/kg bw/d was set. In 1998, the TDI was re-evaluated to 1-4 pg TEQ/kg bw/d. This was based on a number of animal studies that associated TCDD to a number of effects such as neurobehavioral toxicity, immunotoxicity, reproductive toxicity and endometriosis. The approach taken was to estimate body burdens for these effects and, with the use of a one-compartmental kinetic model taking into account an elimination half life in humans and an assumed fraction absorbed from food, an estimated daily intake was calculated for a chronic daily intake which would
lead to body burdens in humans that were similar to those calculated in animals. A composite Uncertainty Factor (UF) of 10 was also applied to this result, which led to the TDI that was established.

7. The Scientific Committee for Food established a TWI of 14 pg TEQ/kg bw for dioxins and dioxin-like compounds in 2001. They used the 1998 WHO evaluation as a basis for the risk assessment and considered new studies. The new studies revealed a particular sensitivity of the gestation day 15 (GD15) rat embryo to TCDD (Faqi et al, 1998; Oshako et al, 2001). The TDI was based on the study that was performed on Wistar rats (Oshako et al., 2001), the most sensitive rat strain, and using the assumptions from the WHO 1998 study regarding absorption from food and half-life. A factor of 2.6 was applied to correct for the high exposure of the fetus following a single acute GD15 maternal dose as opposed to chronic maternal exposure at lower levels. The TDI was set by applying an UF of 3 for NOAEL to LOAEL extrapolation and a factor of 3.2 for interindividual variations in toxicokinetics within the human population.

8. In their evaluation in 2001, the Joint Expert Committee on Food Additives (JECFA) established Provisional Tolerable Monthly Intake of 70 pg WHO TEQ/kg bw. This was based on the same studies as those used by the SCF and taking into account both the Faqui et al. and the Oshako et al. studies when deriving a Health Based Guidance Value (HBGV). Furthermore, a factor of 1.7 instead of 2.6 was used in order to correct for acute maternal exposure. The same UF as the SCF were applied, however PTMI was calculated because JECFA considered that the tolerable intake should be assessed over a period of at least one month.

9. In line with the above evaluations, the COT in 2001 recommended that a tolerable daily intake of 2 pg WHO-TEQ/kg bw per day was established, based upon effects on the developing male reproductive system mediated via the maternal body burden. They considered that that TDI would be adequate to protect against other possible effects, such as cancer and cardiovascular effects. In 2007, the Committee discussed the FSA funded Dioxins Risk Assessment project (T01034). The Committee had previously identified gaps in knowledge related to the risk assessment of dioxins during pregnancy. In light of this, the FSA commissioned a developmental toxicity study, aiming to relate dose of TCDD to maternal burden, fetal burden and biological endpoints. Due to the complexity of TCDD toxicokinetics, it was considered essential to have both an acute dose study, so as to be directly comparable with previous studies which dosed on GD15 (50, 200 or 1000 ng of TCDD/kg bw) and a sub-chronic repeat dose dietary study which was more representative of human exposure to TCDD, in which the female pregnant Wistar (Han) rats were dosed in the diet with 28, 93 or 530 ng TCDD/kg diet(Bell et al., 2007a,b).

10. A significant delay in balano-preputial separation (BPS), a marker of puberty, was observed in the offspring of the highest dose group of the acute study. In the sub-chronic study, delay to BPS was also observed in the lowest dose group, the
dose which was considered the LOAEL for the study. The maternal steady-state body burden for that dose group was determined analytically to be very similar to that calculated for the Faqi study, which was used in the 2001 risk assessment.

11. The Committee noted that doses which gave rise to similar maternal and fetal body burdens resulted in a greater delay in BPS in the sub-chronic study in comparison to the acute exposure. They considered that the difference in magnitude of the effect highlighted the uncertainty regarding the critical window of exposure in the rat. In the absence of robust data relating to the critical window of exposure, the Committee decided that it was appropriate to assume that the effects occurred \textit{in utero}, since basic modelling of rat and human TCDD toxicokinetics indicated that that would result in a more conservative risk assessment.

12. Finally, they concluded that the LOAEL body burden from the FSA funded study provided additional evidence that the TDI of 2 pg/kg bw/day is protective for the developing male fetus and therefore review of the TDI was not a priority on the basis of that study. (COT Statement 2007/02)

13. The U.S. Environment Protection Agency (EPA) in 2012 published an assessment of the non-cancer endpoints for dioxins and established a reference dose of 0.7 pg kg bw/d for 2,3,7,8-tetrachlorodibenzo-\textit{p}-dioxin (TCDD). This was based on data from the two cohort studies of the Seveso incident. One study indicated that men exposed in childhood showed a reduced sperm count and motility (Mocarelli et al., 2008). TCDD levels were measured in blood taken from the boys within one year after the incident. The study indicated a LOAEL of 68 pg/g fat which was used as one of the points of departure (POD). The other POD was based on elevated levels of thyroid-stimulating hormone (TSH) observed in 3-dayold neonates born to mothers from Seveso exposed during the incident (Baccarelli et al., 2008). In this case, TCDD concentrations measured in maternal blood were used to establish a LOAEL of 235 pg/g fat for the effect on TSH in the neonates. The maternal blood samples were taken 16.5 to 22 years after the incident, and TCDD levels higher than 10 pg/g fat were extrapolated to the time of conception. For TSH levels in blood of neonates, a benchmark of 5 IU/mL established by WHO for medical follow-up for potential congenital hypothyroidism was used as a cut-off. Using a physiologically based pharmacokinetic (PBPK) model for humans, the daily TCDD exposures leading to these critical blood concentrations in either boys or mothers were derived. In the case of the boys, it was argued by US-EPA that it was unclear whether the effects on sperm were due to the peak in the blood just after the incident, or the average blood levels during the years before the boys reached the age of 10 (on average 3.5 years). Therefore, both the initial peak level of TCDD and the level some years after the incident were estimated and the average taken as the POD. For both the effects on sperm and TSH, the PBPK model showed that the levels corresponding to the PODs would be obtained with a continuous daily intake of 20 pg/kg bw per day. An UF of 30 (10 to derive a NOAEL and 3 for intraspecies
differences) was used to derive the above-mentioned oral RfD of 0.7 pg/kg bw per day. US-EPA did not estimate the exposure to PCDD/Fs and DL-PCBs.

14. Finally, the U.S. Agency for Toxic Substances and Disease Registry/ Centre for Disease Control and Prevention (ATSDR) have established a chronic duration oral Minimal Risk Level of 1 pg/kg bw for TCDD based on a LOAEL for thymic effects in guinea pigs.

Summary of 2018 EFSA evaluation

Toxicokinetics

15. In humans PCDD/Fs and DL-PCBs are well absorbed and subsequently distributed to liver and body lipids. Levels of the more relevant congeners in blood are in equilibrium with those in adipose tissue. At high exposure, PCDD/Fs and DL-PCBs can show higher lipid-based levels in liver than in adipose tissue. In animal knockout models this has been shown to be due to binding to CYP1A2 in the liver.

16. PCDD/Fs and DL-PCBs are transferred to the fetus from the mother in utero and postnatally via breast milk.

17. Most PCDD/Fs and DL-PCBs are poorly metabolised but some hydroxylated metabolites have been identified. In high doses biotransformation enzymes such as CYP1A1 and 1A2 are induced that likely contribute to the lower half-lives observed in cases of highly exposed people. These metabolites have been detected in both faeces and urine.

18. Compared to laboratory animals, most PCDD/Fs and DL-PCBs show long half-lives (several years) which vary between congeners and depending on the levels, age, BMI and sex.

Toxicity

19. An extensive literature search was performed to identify studies on the adverse effects of PCDD/Fs and DL-PCBs in experimental animals as well as in humans. followed by a selection for relevance according to eligibility criteria and data extraction as outlined in Annex A.1 and sections 3.1.2 and 3.1.4 of the Opinion.

Observations in animals

20. The CONTAM Panel only considered studies that were not evaluated by the SCF in 2001 and that could potentially show effects at lower body burdens than that used to establish the TWI (LOAEL of 40ng/g bw) in their assessment. Only studies in which TCDD was dosed were selected. These included rodent and primate studies.
21. The rodent studies confirmed that various effects were seen at body burdens in a similar range to the ones which the SCF based its previous risk assessment on. These effects included male reproductive effects, effects on embryonic loss, on bones and hepatopathy. The lowest estimated body burdens related to adverse effects (i.e. LOAEL) were 25 ng/kg bw for reduced sperm production (Faqi et al., 1998), delayed puberty development at LOAEL body burden of 42-50 ng/kg bw (Bell, 2007a). Altered bone parameters (Jämäsä et al., 2001) and hepatopathy (NTP, 2006) were observed at NOAEL body burdens of 28 ng/kg bw and 26 ng/kg bw respectively. The lowest NOAEL body burden reported was 9 ng/kg bw based on embryonic loss (Li et al., 2006), however the CONTAM panel noted the large gaps between the dosing groups which could mean that the NOAEL is actually much higher.

22. In primates, dental effects and effects on sperm counts were reported in the high dose groups (up to 420 ng/kg bw). The Panel noted that in several parts of the studies only a few adult animals and offspring were used for each determination of effects, without the criteria being described. Moreover, survival rates for both control and treated groups were low and therefore the Panel concluded that primate studies were not suitable for HBGV derivation.

**Observations in humans**

23. The CONTAM Panel selected studies in humans which analysed in tissues (e.g. blood, human milk, adipose tissue) of the subjects under study for either (i) TCDD or any other congener dominating the TEQ, e.g. due to a contamination incident, (ii) the 17 PCDD/Fs and 12 DL-PCBs, (iii) the 17 PCDD/Fs and 4 non-ortho DL-PCBs, (iv) the 17 PCDD/Fs and 3 non-ortho DL-PCBs (including PCB-126), or (v) the total TEQs (or BEQs analysed by, e.g. CALUX). Studies assessing dietary exposure with validated methods in relation to outcomes were also included.

24. The epidemiological studies have been conducted in subjects/cohorts exposed to PCDD/Fs and DL-PCBs at different life stages under different exposure conditions, e.g. from industrial accidents such as the Seveso Cohort or contamination incidents (Yusho or Yucheng Cohorts), from occupational exposure (chemical workers or military personnel serving in the Vietnam War) or from background levels mainly via the diet in the general population (Duisburg Cohort, Russian Children’s study and others). More information on these cohorts is provided in Section 3.1.4 of the Opinion. Several outcomes have been investigated and the findings on each are outlined below.

25. Chloracne was the most prevalent outcome associated with accidental, occupational or unresolved cases of poisoning, however it only occurs after very high exposures and therefore was not considered relevant for derivation of an HBGV.

26. Associations between exposure to TCDD during infancy/prepuberty and impaired semen quality were observed in three prospective studies (two after the
Seveso incident and one from the Russian Children’s Study). Based on weight of evidence, including also experimental animal studies, the associations were considered causal. The Panel highlighted that in humans the hormonal activity of the testes and the hypothalamic pituitary axis is high for approximately 6 months after birth in boys in a period also referred to as “mini-puberty”. The levels of FSH and LH are high during the first three months of life. LH induces the Leydig cells to proliferate and produce testosterone, which peak between one and three months of life. Induced by FSH, the Sertoli cells proliferate and the Inhibin-B production increases. To some extent, the gonocytes also proliferate in this period. After the mini-puberty, the hypothalamic–pituitary–gonadal axis is quiescent until the onset of puberty, by a poorly understood mechanism. They noted that prenatal and early postnatal period as well as the puberty are sensitive to endocrine disrupting chemicals such as TCDD.

27. With regards to male reproductive effects, impaired semen quality was observed in males in Seveso but only in those that were prepubertal at the time of the incident. Even in the lowest quartile the serum levels of TCDD were high compared to present-day levels in Europe. In another study on adult men born to mothers that were exposed during the Seveso incident, impaired semen quality was observed only in those who had been breastfed. These were accompanied by lower serum Inhibin-B and higher serum FSH concentrations at adult age. In contrast, oestradiol, testosterone and LH levels were unaffected. It could not be deduced whether hormonal effects were cause or consequence of the affected sperm parameters, and no changes in Inhibin-B and FSH were observed in other studies.

28. Together, the Panel considered that this evidence indicated that there may be a postnatal period of sensitivity that might expand into puberty.

29. In the Russian Children’s Study, which included boys exposed to high environmental background levels, associations of serum TCDD with impaired semen quality were observed. Significant associations were observed also for the sum of PCDD-TEQ and PCDFs-TEQ, but not for DL-PCB-TEQ or total TEQ. The association between TCDD and semen parameters became slightly stronger after adjustment for NDL-PCBs but were not changed by adjustment for exposure to organochlorine pesticides.

30. There was insufficient evidence for an association between PCDD/Fs or DL-PCBs and cryptorchidism. For changes in time of pubertal onset and sexual maturity, observed in the Russian Children’s Study, there was insufficient information to conclude on causal associations.

31. In females, for endometriosis, the only available prospective study did not observe a dose response. Moreover, the available case–control studies indicating associations had limitations, therefore the available evidence was insufficient to be used as a basis for the risk assessment. The few available studies indicated no association between exposure and pubertal development. Finally, the evidence was
insufficient for other female reproductive effects (menstrual cycle characteristics, ovarian function, time to pregnancy, uterine leiomyoma, and age at menopause).

32. For birth outcomes, a relationship between high TCDD exposure in fathers and lower sex ratio in offspring (lower number of boys relative to girls), was consistently observed across three different cohorts, was considered likely to be causal. The studies on other birth outcomes (birth weight, preterm birth, fetal Yusho disease and anogenital distance) were inconclusive and could not be used as a basis for the risk assessment.

33. In adults, epidemiological studies provided insufficient support for an association between TCDD, other PCDDs, PCDFs or DL-PCBs and thyroid disease or thyroid function. A study in children born to mothers highly exposed to TCDD in Seveso indicated a causal association between TCDD and increased neonatal TSH. Studies with low-moderate exposure to TCDD, other PCDDs, PCDFs or DL-PCBs did not suggest any adverse effects on the thyroid.

34. Studies were inconclusive on Type 2 diabetes and obesity.

35. An epidemiological study of very high occupational exposure to TCDD (serum TCDD > 1,000 pg/g fat) indicated increased risk of cardiovascular mortality, however at lower exposures to TCDD, other PCDDs, PCDFs or DL-PCBs, epidemiological studies provided insufficient support for an association with cardiovascular risk.

36. Following accidental or occupational exposure, evidence for a causal association with hepatic or digestive diseases was insufficient.

37. Some studies suggested adverse effects on the immune system at background exposure during development, but the available studies did not provide sufficient evidence for an association between PCDD/Fs or DL-PCBs and the functionality of the immune system.

38. Various neurodevelopmental outcomes at different ages were investigated in children, but few outcomes were assessed in several cohorts and/or at similar age. The available information was not considered sufficient to form a basis for the risk assessment. There was insufficient information to draw conclusions on effects on the nervous system after exposure in adult life.

39. In three different population groups, childhood exposure to TCDD and/or other PCDD/Fs was dose-relatedly associated with tooth enamel hypomineralisation or enamel defects. Hypomineralisation of permanent teeth was considered likely to be causally related to exposure and was likely to be a postnatal effect. Limited evidence from one cohort indicates associations between PCDD/F and DL-PCB exposure and some changes in bone parameters.

40. Finally, with regards to cancer, several studies (many with multiple co-exposures) showed a positive association with all cancers, however combined there was no clear link to any specific cancer site. There was no clear dose–response relationship between exposure and cancer development.
Critical effects, dose-response assessment and derivation of an health-based guidance value

41. The CONTAM Panel decided to base its assessment on human studies and also evaluate the relevant studies in experimental animals in support of the epidemiological studies.

42. Among the endpoints investigated, effects on sperm quality were selected for the selection of a reference point for the derivation of a HBGV.

43. Three studies, two on the Seveso population and one from the Russian Children’s study were available. There were differences between the exposures in the three studies and PCDD/Fs and DL-PCBs exposure was only taken into account in the Russian Children’s study. These are discussed in detail in Section 3.1.7 of the Opinion.

44. The narrow age range, the fact that two semen samples were collected in the Russian Children’s study as well as being collected in a laboratory as opposed to the Seveso studies in which the samples were collected at home were some of the advantages of the Russian Children’s study (elaborated in section 3.1.8.1 of the Opinion). In the exposed groups in Seveso, sperm concentrations were decreased by about 30% and 60%. In the boys from the Russian Children’s Study the reduction was about 40%. However, in this study, the decrease in sperm concentration occurred already at a PCDD/F-TEQ level of 11 pg/g fat (LOAEL), with no further decrease at higher levels. The study showed effects at the lowest serum levels, with a NOAEL of 7.0 pg WHO$_{2005}$-TEQ/g fat for the sum of PCDD/F TEQ, which was the median in the lowest quartile. However, no significant association was observed when including also the Co-PCB-TEQ$^1$ which the Panel considered that it may be related to a much lower potency of PCB-126 in humans than expressed by the current WHO$_{2005}$-TEF.

45. An additional possibility was effects of co-exposure to Non Dioxin Like PCBs, since the associations between TCDD or total TEQ and semen parameters became slightly stronger after adjustment for these, although there were no significant association between NDL-PCBs and semen parameters. Therefore, the CONTAM Panel only evaluated the association with PCDD/F-TEQ levels. For these levels, the median values in quartiles 2–4 were 10.9, 15.9 and 32.8 pg WHO$_{2005}$-TEQ/ g fat, respectively. The mean sperm concentration in the lowest quartile of PCDD/F-TEQ was 64 million/mL and the mean levels in quartile 2–4 were about 40 million/mL. This difference was considered biologically relevant.

46. In the Seveso studies, sperm concentrations differed between exposed and control groups with much higher estimated TCDD, PCDD/F-TEQ, and total TEQ

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$^1$ PCB-77,8-81, -126 and -169
levels with an apparent NOAEL level higher than the LOAEL level in the Russian
Children’s Study.

47. The CONTAM Panel decided to use the NOAEL of the Russian Children’s
study of a median serum level of 7.0 pg WHO2005-TEQ/g fat for the sum of PCDD/F
TEQ in the lowest quartile as reference point for the HBGV and for derivation of the
human exposure associated with this serum concentration at the age of 9 years.

48. When considering modelling in order to estimate the intake leading to the
critical body burden (Section 3.1.8.2 of the Opinion) several options were
considered. It was noted that since the SCF evaluation, several physiological models
have been developed that take into account not only accumulation in body fat, but
also induction of liver CYP enzymes, liver sequestration and growth.

49. The Panel noted that induction of liver enzymes results in increased clearance
and reduced half-life at higher body burdens. Growth will result in the ‘dilution’ of the
existing body burden and thus an apparent shorter half-life in children. Since the
most critical effect was observed in boys exposed before the age of 10 years, i.e.
reduced sperm concentrations, a model including growth was considered more
suitable.

50. Furthermore, levels in milk and the duration of breastfeeding influence the
serum level and body burden in children, which they considered that it needed to be
taken into account when estimating the daily human intake leading to the critical
serum concentration. In addition, infants are already exposed in utero and will have a
starting level at birth depending on the body burden of the mother.

51. For the modelling, it was decided to use an age of 35 years for mothers, in
order to cover a common age for having the first child. However, it was mentioned
the actual increase in serum levels at child-bearing age is rather minor.

52. The Panel evaluated two models. The first one was the model for TCDD
developed by Emond et al. (2005) was evaluated by transferring the ACSLX codes
into Berkeley-Madonna, and subsequently into R. The adaptations for including a
breastfeeding period (Emond et al., 2016) were also evaluated but that model
seemed to require further investigation. The CONTAM panel noted that there were
several discrepancies between the calculations from the model and data reported on
human levels (section 3.8.1.2 of the Opinion).

53. The second model evaluated was the Concentration and Age-Dependent
Model (CADM). This was developed by Carrier et al. (1995) and optimised by
Aylward et al. (2005). The original model takes into account liver sequestration, but
was optimised by including the loss of TCDD ‘due to simple lipid partitioning from the
circulation across the intestinal lumen into fecal contents’, based on the studies by
Moser and McLachlan (1999). This model was further adapted by Ruiz et al. (2014)
to include a growth curve and a breastfeeding period. These model codes for
Berkeley Madonna were implemented and evaluated.
54. The CADM model was developed for TCDD and estimates the levels in the fat compartment (lipid based), liver (wet weight) and total body (wet weight), the latter based on relative fractions of 25% and 3% of the body weight for the fat compartment and the liver. Blood levels are not predicted by the model but can be assumed to be similar to those in adipose tissue when adjusted for lipid. Once absorbed, TCDD distributes between liver and fat taking into account induction of CYP1A2 enzyme.

53. A number of issues were identified and the model was modified accordingly by the CONTAM Panel (Appendix E for model codes), regarding growth curves, adjustment of units for exposure after the breastfeeding period, milk intake when breastfeeding, absorption constant for infants, half-life in infants and body burden at birth (Section 3.1.8.2 of the Opinion).

54. Using this modified model and the NOAEL from the Russian Children’s study, the CADM simulations indicated that following breastfeeding for 12 months, and a similar intake of sons after breastfeeding as for mothers, the intake should be below 0.3 pg TEQ/kg bw per day in order not to reach a serum concentration of 7.0 pg PCDD/F-WHO2005-TEQ/g fat at 9 years of age.

55. When taking into account 12 months breastfeeding followed by twofold higher intake by boys than by adults, the intake by the mothers should be below 0.25 pg PCDD/F-WHO2005-TEQ/kg bw per day.

56. Considering the above, the Panel concluded that the data suggested that the long-term intake should remain below 0.25 pg WHO2005-TEQ/kg bw per day or 1.75 pg WHO2005-TEQ/kg bw per week to ensure that serum levels in boys remain below the NOAEL for effects on sperm concentrations of 7.0 pg WHO2005-TEQ/g fat, also when breastfed for 12 months. The value of 1.75 was rounded to 2 considering the uncertainty in the estimation of the critical serum level and corresponding daily intake. The Panel decided not to apply additional UFs, since the HBGV was based on a NOAEL obtained in a study with a relatively large number of boys (n = 133) and repeated semen sampling.

57. Therefore, a TWI was established of 2 pg WHO2005-TEQ/kg bw per week.

58. Although the TWI is based on findings on PCDD/F-TEQ only, the CONTAM Panel concluded that the TWI should apply to the sum of PCDD/Fs and DL-PCBs. However, they highlighted that the studies indicated that the current TEFs require re-evaluation. In particular, PCB-126, which contributes most to the DL-PCB-TEQ level, may be less potent in humans than indicated by the TEF-value of 0.1 (Section 3.1.7.2.1 of the Opinion).

59. The CONTAM Panel noted that the TWI is based on serum levels sampled from boys at the age of 8–9 years, however critical window for the effects on sperm may actually be at younger age or during puberty. The TWI was considered protective for the general population and that it would prevent women from reaching a concentration in the blood that could lead to harmful pre- and postnatal effects.
They noted that modelling of concentrations in serum took into account the much higher exposure during infancy from both breast milk and food. The CONTAM Panel therefore considered the modelling sufficiently accurate as there were no indications that the serum levels in the boys from the Russian Children’s Study during the first 9 years would have followed a different pattern than predicted by the model.

60. Based on the available data, they concluded that the TWI should be protective towards all endpoints. These include lower sex ratio, higher TSH levels in newborns and developmental enamel defects on teeth, the latter appearing to occur at only slightly higher exposure than the developmental effects on semen quality.

Risk Characterisation based on the new TWI

61. This section briefly describes EFSA’s human risk characterisation based on the TWI of 2 pg WHO2005-TEQ/kg bw per week. Details on exposure assessments are given in Section 3.3 of the Opinion.

62. Current exposures were evaluated using mean levels for PCDD/Fs or the sum of PCDD/Fs and DL-PCBs in various food groups, expressed in WHO2005-TEQs. This was performed using the different food consumption surveys from European countries, taking into account different age classes. The exposure was subsequently compared with the newly established TWI of 2 pg TEQ/kg bw per week. Since the exposure was estimated on a daily basis, the values were first extrapolated to a weekly basis, simply by multiplication with a factor of 7.

63. The tables below summarise the current exposures in different population groups:

Table 1: Weekly intake of the sum of PCDD/Fs and DL-PCBs (29 congeners)

<table>
<thead>
<tr>
<th>Age class</th>
<th>N</th>
<th>Minimum</th>
<th>Median</th>
<th>Maximum</th>
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<td></td>
<td>LB UB</td>
<td>LB UB</td>
<td>LB UB</td>
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<tr>
<td>Infants(c)</td>
<td>6</td>
<td>3.1 4.6</td>
<td>4.6 6.5</td>
<td>8.1 9.9</td>
</tr>
<tr>
<td>Toddlers</td>
<td>10</td>
<td>4.8 6.2</td>
<td>8.8 10.7</td>
<td>14.8 18</td>
</tr>
<tr>
<td>Other children</td>
<td>18</td>
<td>3.9 5</td>
<td>8.1 9.7</td>
<td>14.1 17.2</td>
</tr>
<tr>
<td>Adolescents</td>
<td>17</td>
<td>2.1 2.7</td>
<td>4.6 5.5</td>
<td>8.9 10.5</td>
</tr>
<tr>
<td>Adults</td>
<td>17</td>
<td>2.9 3.4</td>
<td>4.5 5.3</td>
<td>7.8 9.1</td>
</tr>
<tr>
<td>Elderly</td>
<td>14</td>
<td>2.7 3.6</td>
<td>4.7 5.4</td>
<td>8.9 9.6</td>
</tr>
<tr>
<td>Very elderly</td>
<td>12</td>
<td>3 4</td>
<td>4.5 5.1</td>
<td>8.5 9.2</td>
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<table>
<thead>
<tr>
<th>Age class</th>
<th>N</th>
<th>95th percentile dietary exposure (pg WHO2005-TEQ/kg bw per week)</th>
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<tr>
<td></td>
<td></td>
<td>Minimum</td>
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64. In comparison to the sum of PCDD/Fs and DL-PCBs, the exposure to PCDD/F-TEQ only (17 congeners) was, in general, a factor 2.4 lower for the mean and a factor 2.7 lower for the P95 exposure. These are summarised in Table 2 below.

Table 2: Weekly intake of PCDD/Fs (17 congeners)

<table>
<thead>
<tr>
<th>Age class</th>
<th>N</th>
<th>Minimum dietary exposure (pg WHO2005-TEQ/kg bw per week)</th>
<th>Median</th>
<th>Maximum</th>
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<tr>
<td></td>
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<td>LB</td>
<td>UB</td>
<td>LB</td>
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<td>Infants(c)</td>
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<td>2</td>
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<td>Toddlers</td>
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<td>2</td>
<td>3.2</td>
<td>3.6</td>
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<tr>
<td>Other children</td>
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<td>2.8</td>
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<td>17</td>
<td>0.8</td>
<td>1.2</td>
<td>1.7</td>
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<tr>
<td>Adults</td>
<td>17</td>
<td>1</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Elderly</td>
<td>14</td>
<td>1.3</td>
<td>1.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Very elderly</td>
<td>12</td>
<td>1.4</td>
<td>1.9</td>
<td>1.6</td>
</tr>
</tbody>
</table>

65. It was concluded that the intake of PCDD/Fs and DL-PCBs by Adolescents, Adults, Elderly and Very Elderly for all mean and P95 estimates exceeds the TWI of 2 pg TEQ/kg bw per week, by up to a factor 15.
66. For Toddlers and Other Children, the exceedances are approximately a factor of 2 higher than in the older age groups. The Panel considered that since higher exposure at young age was taken into account when deriving the TWI, the exceedances were in a similar range to the older age groups.

67. The Panel noted that intake of PCDD/F-TEQs was more than twofold lower than the intake of total TEQs (sum of PCDD/Fs and DL-PCBs). As a result, only part of the mean exposure exceeds the TWI, but were estimated P95 intakes are higher than the TWI, by up to a factor 5.7 when focussing on Adolescents, Adults, Elderly and Very Elderly. They considered the difference between LB and UB estimates to be rather small and that the exceedance were not due to a high fraction of left-censored data and too high LOQs.

68. Based on the above, the CONTAM Panel concluded that the current exposure to PCDD/Fs and DL-PCBs is of concern.

69. The Members are invited to read the Opinion and Annex attached as Annexes on this paper and comment on the approach used by EFSA.

Questions to the Committee

i. Does the Committee agree with the selection of the critical study for the derivation of an HBGV?
ii. Do the Members agree on the model used by EFSA for the derivation of an HBGV?
iii. Do the members agree with EFSA’s considerations regarding potential differences in relative potencies and the current TEF values for PCDD/Fs and DL-PCBs?
iv. Do the members agree on the TWI established?
v. Do the Members have any further comments?

Secretariat

October 2018
This is a background paper for discussion.
It does not reflect the views of the Committee and should not be cited.

References:


• Li B, Liu HY, Dai LJ, Lu JC, Yang ZM and Huang L, 2006. The early embryo loss caused by 2,3,7,8-tetrachlorodibenzo-p-dioxin may be related to the accumulation of this compound in the uterus. Reproductive Toxicology, 21, 301–306.


COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Discussion paper on the EFSA Opinion on “Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food.”

This Annex contains the EFSA Opinion “Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food.”

Note: At the time this paper was sent out to Members the EFSA Opinion had not been published and therefore this paper and its annexes will not be put onto the website until the EFSA Opinion is published.

A copy of the EFSA Opinion, which the FSA has access to, has been emailed or posted out to all Members with this paper.