Committee Procedures - 2022

In this guide

Response to EFSA consultation on “Re-evaluation of the risks to public health from bisphenol A (BPA) in foodstuffs”

1.75 In December 2021, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) published a draft opinion re-evaluating the health risks arising from the presence of bisphenol A (BPA) in food. The panel proposed a significant reduction to the current temporary Tolerable Daily Intake (TDI) of 4 µg/kg body weight (bw) to 0.04 ng/kg bw. This reduction would mean that both mean and high level consumers for all age groups would exceed the new TDI by 2-4 orders of magnitude.

1.76 Due to the size and complexity of the draft opinion, the COT held an extraordinary meeting to discuss it, before feedback was then provided to EFSA as part of their consultation process. The Committee considered the Health Outcome Category (HOC)/cluster approach used by the EFSA CEP panel to conduct the evaluation comparing it to the approach taken by the COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence subgroup (SETE). The Committee also discussed the benchmark dose modelling used by EFSA including the uncertainty analysis and derivation of the Health Based Guidance Value (HBGV). The Committee then considered the toxicokinetics along with the specific endpoints of immunotoxicity, reproductive and developmental toxicity, neurotoxicity and developmental neurotoxicity, genotoxicity, and other minor endpoints; the approach to epidemiology, metabolic effects, cardiotoxicity, and carcinogenicity.

1.77 The comments agreed by the Committee were submitted to EFSA as part of their public consultation process. The final EFSA opinion is expected to be published towards the end of 2022.

EFSA Draft Opinion for Public Consultation on “Re-evaluation of the existing health-based guidance values for copper and exposure assessment from all sources

1.78 The European Food Safety Authority Scientific Committee were asked by the European Commission to review the existing scientific evidence and all new relevant studies with the aims:

- to provide a scientific opinion on an ADI for copper which can be used as a reference value for copper containing regulated products.

- to take into account all sources of exposure and integrate different approaches and scenarios, to perform a new estimation of the overall copper intake which includes contributions from all major sources of exposure.

1.79 The Committee considered the approach used by the EFSA Scientific Committee to establish the Acceptable Daily Intake (ADI) for copper and the studies used by the Scientific Committee to reach their conclusions. The pivotal studies used by EFSA to determine the HBGV were Turnlund et al., (2005) and Harvey et al., (2003) which examined copper homeostasis. The Committee discussed these studies and highlighted that there was a limited number of participants which were all male that could have an impact on the reliability of the HBGV. However, it was noted that the homeostatic response would not vary in relation to age, sex or pregnancy.

1.80 In conclusion, the Committee agreed that EFSA's proposed new HBGV of 5 mg per day and the harmonised approach used to establish it were acceptable.

1.81 The comments agreed by the Committee were submitted to EFSA as part of their public consultation process.

Draft FSA/HSE/VMD report on approaches to chronic dietary exposure assessment for chemicals in food

1.82 The COT was asked to comment on a report drafted by FSA, the Health and Safety Executive (HSE) and the Veterinary Medicines Directorate (VMD) on approaches to chronic dietary exposure assessment for chemicals in food. The draft report was also being taken to the Expert Committee on Pesticides (ECP) and the Expert Committee on Pesticide Residues in Food (PRiF) for comment before being finalised.

1.83 The work had been undertaken because there were differences in the current approaches to chronic dietary exposure assessments undertaken by the HSE for pesticides, VMD for veterinary medicines and FSA for chemical contaminants and other chemicals in food. Furthermore, there were differences in how these assessments were conducted internationally for pesticides and emerging differences for veterinary medicines. In addition, following exit from the EU, it was timely for UK regulators to consider the approaches they might wish to take in the future.

1.84 The draft report discussed the principles of dietary exposure assessments and described the current approaches to chronic dietary exposure

assessments being taken by the FSA and for pesticides and veterinary medicines. It discussed the current differences in approach and the reasons for them, uncertainties in exposure assessments, considered the possibilities for common approaches to be taken in the future and the approaches to substances with multiple uses (e.g. as both pesticides and veterinary medicines). It also included some considerations on cumulative and aggregate exposure assessment and referred to the recent considerations of less than lifetime and variable exposure over a lifetime by the COT and COC.

1.85 The draft report made a number of recommendations. These included increasing collaboration between FSA, HSE and VMD on topics such as exposure assessments for substances with multiple uses, the setting of common Maximum Residue Levels (MRLs) and Health Based Guidance Values (HBGVs), and on methodologies for cumulative risk assessments; continuing international collaborations; periodically reviewing exposure assessment methodologies for fitness for purpose and considering their uncertainties; and having up-to-date comprehensive food consumption data, which are contained within a central database to which staff from each of the departments/agencies have access and training on their use.

1.86 The COT advised that the recommendations be separated out from the conclusions. The FSA’s approach was noted to be usually closer to actual consumer exposures compared to regulatory approaches for approvals of pesticides and veterinary medicines. If joint exposure assessments were to be performed it would need to be agreed what degree of conservatism there should be. The COT supported the desire for more information on cumulative and aggregate exposures but the methods were not fully developed yet and there were still improvements that could and should be made to exposure assessments for single substances first. Probabilistic modelling was included in the report as a high tier model but that was not being conducted to much extent at the moment, though the software was available and it could be used more. There was also agreement with the recommendation of a central database for food consumption data.

1.87 The COT considered that it was a good idea to conduct exposure assessments more consistently across chemical areas; however, it was noted that for applicants there was also the international consideration and to them it would be preferable for there to not be too many differences in the approaches used between regions internationally, e.g. between the UK and Europe.

1.88 The COT noted that EFSA had taken one approach to the cumulative risk assessments of pesticides and a different approach to other chemicals. While they had produced guidance it was not clear whether they were currently routinely undertaking cumulative risk assessments for chemicals other than pesticides. Where such cumulative risk assessments had been performed, a constrained approach tended to have been taken, for example, grouping chemicals in the same regulatory area that have similar structures. At present, there did not appear to be have been any move to conder, for example, all chemicals across all sectors that cause hepatic steatosis as a single group, for regulatory purposes. The COT suggested that the report should recognise the difficulties as well as the possibilities of performing combined exposure assessments across different regulatory areas.

1.89 The COT observed differences in the age ranges being used currently to define infants and children, asked for justification for the use of the 97.5th percentile to represent high consumers to be included in the report, and discussed the extent to which the National Diet and Nutrition Survey (NDNS) adequately covered ethnic groups and groups such as vegans. The NDNS reflected the whole population but focused studies would be needed to reflect the consumption patterns of groups that comprise only small percentages of the entire population, to ensure their adequate statistical characterisation.

1.90 It was noted that exposure assessors are constrained by the data that they can obtain. For example, JECFA and JMPR do not have access to consumption data with the level of granularity that the FSA has, and hence would have considerable difficulties in performing probabilistic modelling.

1.91 The draft report would be revised and published after the ECP and PRiF had also commented.

Statement on the EFSA Opinion on the risks to human health related to the presence of perfluoroalkyl substances in food

1.92 The European Food Safety Authority (EFSA) was asked, by the European Commission, to prepare an Opinion on the risks to human health related to the presence of perfluoroalkylated substances (PFASs) in food, and to consider existing hazard assessments and available occurrence data. The statement was published in September 2020.

1.93 The Committee on Toxicity of Chemicals in Food, Consumer products and the Environment (COT) have reviewed the “EFSA Opinion Risk to human health

related to the presence of perfluoroalkyl substances in food" (2020) alongside UK exposure data to assess the potential risks to the UK population from PFASs (predominantly through exposure via the diet).

1.94 Per- and polyfluoroalkyl substances (PFASs) with a minimum of six carbons in their backbone, are a class of over 12,000 fluorinated substances (US EPA CompTox Dashboard 2022). They have been produced since the 1940s and are, or have been, used in a broad range of consumer products and industrial applications (Glüge *et al*., 2020). Their structure enhances their utility in a variety of applications including the production of water- and oil-resistant clothing, electronics, non-stick cookware, carpets, and food packaging materials.

1.95 Many PFASs are environmentally long-lived and individuals are exposed to them through all environmental sources, i.e. drinking water, air, dust, and the diet and through the placenta and breastfeeding for developing offspring (Sunderland *et al*., 2019).

1.96 The tolerable weekly intake (TWI) was established by EFSA based on epidemiological studies of an effect on the immune system, as this was considered, by the EFSA CONTAM Panel, to be the critical effect. Two studies on this (Abraham *et al*., 2020 and Grandjean *et al*., 2012) were considered by EFSA as suitable for hazard characterisation. One of these studies, Abraham *et al.* (2020), was amenable to dose-response modelling (i.e. analysis of the response of an organism, as a function of exposure (or doses) to a chemical after a certain exposure time); which resulted in a benchmark dose limit value (BMDL10) for blood serum of 17.5 ng/mL for the sum of the four main PFASs present. This value was then used as the reference point to calculate the corresponding tolerable daily intake for a mother, to protect their offspring, considered the most sensitive population, which was 0.63 ng/kg body weight (bw) per day. This was then converted to a weekly value, because of the long persistence of PFASs in the body, the TWI, of 4.4 ng/kg bw per week for the sum of the four PFASs PFOS, PFOA, PFHxS and PFNA, for use as the health-based guidance value.

1.97 The COT agreed that, on the basis of the information reviewed by EFSA, qualitatively the appropriate health endpoint had been selected but quantitatively, questioned the calculations. Overall, there were some reservations about the choice of the critical study (Abraham *et al.*, 2020) and the specific effect that was selected. However, the COT agreed that the critical study was the best available; and, in the absence of more appropriate studies, its use was understandable. Therefore, it was not unreasonable that this study was selected.

1.98 The COT had significant reservations about the dose-response model used, including the modelling approach, and the TWI which had been established, due to the uncertainties and the caveats involved.

1.99 The COT agreed that the use of the sum of the four PFASs was acceptable as a first approximation for exposures of PFASs but had reservations about the calculations due to the uncertainties.

1.100 The diet is the predominant route of exposure to PFASs, however, other possible sources of exposure include dust by ingestion and indoor air by inhalation, and these exposures have been considered. There may also be some exposure via the skin, however these have not been calculated.

1.101 The values for the BMDL and TWI were low and there was a lot of uncertainty surrounding the data used by EFSA.

1.102 Estimated breast milk exposures for UK infants all exceed the TWI of 4.4 ng/kg bw per week. However, EFSA cautions that “the higher exposure of breastfed infants is taken into account in the derivation of the TWI (i.e. it is assumed that those later exposed have already received this exposure) and the intake by infants should therefore not be compared with this TWI”.

1.103 Blood serum level modelling of the four PFASs indicates that the lower bound estimates of exposure (assuming that levels below detection are zero) is a more accurate prediction of the exposure than the upper bound estimates (assuming that levels below detection are present at that level), which would lead to a much higher exceedance of the critical blood serum levels. Lower bound mean estimated dietary exposures for adolescents, adults, the elderly and the very elderly approximate the TWI, that for other children is approximately twice the TWI, and for infants and toddlers are several times the TWI.

1.104 Estimated exposures from household dust at average median PFASs concentrations for all UK populations, for individual PFASs, are below the TWI. For exposures estimated from average maximum PFASs concentrations in household dust the TWI is exceeded for PFOS, PFOA and PFHxS by infants, toddlers and children.

1.105 The EFSA CONTAM Panel, in their evaluation of PFASs, assessed exposure both to individual compounds and using a mixtures approach (i.e. a probabilistic model for representing the presence of subpopulations within an overall population, without requiring that an observed data set should identify the sub-population to which an individual observation belongs) for the sum of four PFASs:

PFOS, PFOA, PFHxS and PFNA. All exposure estimates were compared to the TWI of 4.4 ng/kg bw per week. The CONTAM Panel considered that the impact of the uncertainties on the risk assessment for the sum of PFOA, PFNA, PFHxS and PFOS is high.

1.106 The exceedances of the TWI at lower bound exposure estimates indicate a potential health concern.

1.107 Whilst the COT is unable to suggest an alternative TWI at this time due to the lack of data, there are strong caveats when comparing the exposure estimates with the TWI established by EFSA. There is considerable uncertainty as to the appropriateness of the derivation of the TWI and of the biological significance of the response on which it is based.

1.108 The COT suggested that in future reviews it could use the averages for exposures for the four PFASs added together to provide a reasonable estimation of combined PFASs exposure for comparison to the TWI.

1.109 The full statement can be found at: Statement on the EFSA Opinion on the risks to human health related to the presence of perfluoroalkyl substances in food .

Response to draft EFSA opinion on the human health risks related to the presence of N-nitrosamines (N-NAs) in food

1.110 EFSA published a draft Scientific Opinion on the human health risks related to the presence of N-nitrosamines (N-NAs) in food for consultation October 2022. The COT were asked to provide comments on this draft.

1.111 Nitrosamines are the reaction products formed from nitrosating agents, such as nitrites or nitrogen oxides, and amino-based substances, such as secondary amines. They may be formed in a variety of foods (e.g., cured meat products, processed fish, beer and other alcoholic and non-alcoholic beverages, cheese, soy sauce, oils and processed vegetables) under processing conditions in the presence of these reactants.

1.112 It was considered that the draft Opinion provided a good summary in terms of ADME and genotoxicity data. It was commented that the main issues open to question were the method of benchmark dose (BMD) analysis and how compounds were aggregated (grouped).

1.113 Positive feedback was provided on the draft Opinion, which Members considered to be a comprehensive review of the topic. The comments agreed by

the Committee were submitted to EFSA as part of their public consultation process.