Committee Procedures - 2023

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Public consultation on draft EFSA opinion on polybrominated diphenyl ethers (PBDEs)

1.48 In June 2023, EFSA released for public consultation a draft update of its risk assessment of polybrominated diphenyl ethers (PBDEs) in food; PBDEs were previously used as flame retardants in construction materials, furniture, and electric and electronic equipment and are widespread environmental contaminants.

1.49 EFSA had previously published a risk assessment of PBDEs in 2011. In the new assessment, two additional congeners were considered, and a total margin of exposure approach was used. The draft updated assessment concluded that the dietary exposures estimated raised a potential health concern for toddlers, with >70% certainty at mean exposure and >95% certainty at 95th percentile exposure. The Committee were asked to provide comments on the draft opinion to be submitted to EFSA as part of their consultation process.

1.50 The Committee considered the animal data to be generally robust but noted that some significant assumptions had been made. They agreed that neurodevelopmental effects and reproductive toxicity were the critical endpoints. The available epidemiological studies, though robust, were difficult to assess, and the epidemiological evidence was considered to provide less of a signal than the toxicological data.

1.51 The Committee considered that some of the evidence from animal studies for a substance-related effect was questionable, and this should have been considered in the uncertainty analysis. Some of the neurobehavioral changes were very minor and there were major inconsistencies in the neurobehavioral changes reported, which lacked biological plausibility. In a developmental neurotoxicity study conducted according to OECD test guideline 426, a technical PBDE product showed no adverse effects at any dose level, which contrasted greatly with the point of departure identified for its major constituent congener, but there did not appear to be any discussion of this. The Committee

considered that findings in single studies, in particular those without clear dose-response relationships, should be treated with caution, especially when an adequate OECD guideline study identifies no adverse effects.

1.52 Animal studies showed effects on the thyroid and the draft opinion appeared to be trying to link this to thyroid disease in humans, but the Committee considered this a step too far. The effects observed in studies in rats were typical of a liver-thyroid effect seen in rats, with microsomal enzyme induction causing increased clearance of thyroid hormones. The draft opinion did not appear to discuss direct versus indirect effects on the thyroid.

1.53 The Committee found the uncertainty analysis difficult to interpret. It was not considered useful without a rationale being provided and without further information on how the numbers for percent certainty were generated and what they mean. Risks may be overestimated by the body burden approach used when considering the endpoints and susceptible populations and the very long half-lives in humans, which were up to 8 years, and it was unclear how this had been taken into account in the uncertainty analysis.

1.54 The recommendations made in the draft appeared largely pertinent. However, the Committee questioned the objective of some of the recommendations for those PBDEs that are no longer used, e.g., the development of Adverse Outcome Pathways (AOPs), when there was already a significant amount of toxicology and exposure data available, and a risk had been identified.

1.55 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 in early 2024.

Public consultation on draft EFSA opinion on polychlorinated naphthalenes (PCNs) in food and feed

1.56 EFSA released for public consultation a draft opinion on polychlorinated naphthalenes (PCNs) in food and feed in November 2023. PCN mixtures were used in the past in dielectrics, lubricants, electric cable insulation, preservatives of wood, paper and fabric, cutting and grinding fluids, and plasticisers and can also be formed as unintentional byproducts in the production of other industrial chemicals. They are formed by combustion processes including incineration, forest fires and burning of coal. They are lipophilic, bioaccumulative

and occur widely in food and feed. They are considered persistent organic pollutants (POPs) under the Stockholm Convention.

1.57 EFSA's evaluation focused on hexaCNs as there were only very limited data on other PCN congeners. No suitable epidemiological data were identified. The toxicological data were considered insufficient to establish an HBGV and a margin of exposure (MOE) approach was used, based on a BMDL20 for decreased platelet count in a subchronic toxicity study in rats which tested a hexaCN mixture. MOEs for the exposure to hexaCNs were all much greater than 2000, and the draft opinion concluded that these did not raise a health concern. No risk characterisation was performed for animals exposed via feed because suitable points of departure could not be identified for each species. The Committee were asked to provide comments on the draft opinion to be submitted to EFSA as part of their consultation process.

1.58 The Committee largely agreed with the opinion and with the recommendations made and agreed that dietary exposures to hexaCNs are not a concern. Any information on production, environmental persistence, and trends in occurrence levels over the last 10-20 years would be useful. One of the recommendations, on the use of non-animal methods in order to assess risks from feed, was open ended, and clarity would be welcome.

1.59 While the Committee agreed that dietary exposures to hexaCNs are not a concern, it was not clear how the conclusion of 99% certainty of no health concern had been arrived at from the uncertainty analysis conducted. The Committee considered that some clarity and explanation would be useful.

1.60 The Committee could not see why the toxicology data in laboratory animals could not also be used to characterise the risks to animals exposed via feed, allowing for uncertainties as had been done for the human health risk characterisation.

1.61 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 in mid-2024.

Draft EFSA opinion on the Tolerable Upper Level for vitamin B

1.62 The EFSA Food and Nutrition Innovation Unit held a public consultation on their draft opinion on a proposed tolerable upper intake level (TUL) for vitamin B6. The COT were asked to provide comments on the draft opinion to be fed back to EFSA. The TUL was based on the observation of peripheral neuropathy in a study in women being treated for premenstrual syndrome. The Committee agreed that this was the most relevant toxicological endpoint noting that it had been observed in both humans and animals. However, the Lowest Observed Adverse Effect Level (LOAEL) used to derive the TUL and the rationale for the accompanying uncertainty factors needed additional clarification as they might not reflect the full variability of the human pharmacokinetics; additional discussion of the suitability of the TUL for pregnant women would be useful.

1.63 The Committee considered that further clarification of the section on Absorption, Distribution, Metabolism and Excretion (ADME) was needed, as this suggested binding was to the lysine residues of albumin in some parts of the section but noted binding to lysine residues in other proteins in addition to albumin elsewhere in the section.

1.64 The Committee discussed biomarkers of vitamin B6 intake and status, stating it would provide greater context if commentary on the implications of genetic variability, for example in alkaline phosphatase activity, were provided. A recently published paper by Jarett et al (Am J Clin Nutr, 116, 1767-1778, 2022) was cited which showed an interaction between vitamin B6 status and genotype which affected the dose-response. It was agreed that this study should be brought to the attention of EFSA.

1.65 Members commented on the case reports reviewed by EFSA. In particular, the accuracy of the summary for the Dalton and Dalton (1987) study was questioned; the participant was not positively re-challenged but rather symptoms recurred when consumption of the vitamin was resumed.

1.66 It was noted that the recommended range of the health-based guidance value (HBGV) for vitamin B6 was wide; 10-100 mg for adults. This reflected variability, but also choices made in the selection of LOAELs and UFs. A paragraph introducing or providing an explanation of the broad range of HBGVs would be beneficial for context setting and transparency.

1.67 The Committee expressed concern regarding the interpretation of the LOAEL identified in the dog studies which was outlined in the animal data section of the opinion. Members stated that while pathological changes had been observed, there was uncertainty around the measurement of the neurological

endpoints, and it was questioned how sensitive these clinical signs would be.

1.68 It was also highlighted that there seemed to be a mismatch between human and animal data and the comparability of the reproductive toxicity endpoints since the available human data related to effects on women rather than their offspring.

1.69 Members supported the proposed recommendations for further research made by EFSA, in particular those for further studies on toxicogenetics.

1.70 The Committee were of the opinion that further detail on the reason behind EFSA's selection of 50 mg/day Vitamin B6 as the threshold at which peripheral neuropathy occurs was needed, given that the available nutrivigilance data indicted effects at lower doses.

1.71 The Committee made a number of minor editorial comments and suggestions which were also submitted to the consultation.

1.72 The final EFSA opinion is expected to be published later in 2023.

Public consultation on EFSA'S 2023 re-evaluation of the risk to public health from inorganic arsenic in food

1.73 In July 2023, the EFSA Panel on Contaminants in the Food Chain (CONTAM) published a draft opinion re-evaluating the health risks arising from the presence of inorganic arsenic (iAs) in food. EFSA had considered it appropriate to update their assessment as new studies had become available on the toxic effects of iAs, as well as new information on occurrence and exposures. The COT were asked to comment on the draft opinion as part of the EFSA public consultation process.

1.74 The draft opinion was also circulated to Members of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) who provided comments which were combined with those of COT.

1.75 Members agreed that the draft opinion was comprehensive and clearly laid out.

1.76 The Committee noted that a relationship between arsenic and skin lesions is well established, though the mechanism is unclear, and further

information was needed in this area. It was noted that the paper by Diamond-Gilbert (Environ Health Perspectives, 121, 1154-60, 2013) which was discussed by EFSA in this context referred specifically to invasive squamous cell carcinoma. A lot of the data came from human studies in Bangladesh where there were high levels of arsenic in drinking water. It was possible that UV radiation was a co-carcinogen.

1.77 EFSA used a margin of exposure (MOE) approach in their assessment as iAs is considered a genotoxic carcinogen with additional epigenetic effects. While the calculated MOEs raised potential health concerns with respect to skin cancer, supported by the uncertainty analysis, EFSA concluded that they were unable to derive a level of low concern for iAs as the endpoint used was human cancer and there was no EFSA guidance on the use of such an endpoint. The Committee did not accept this view, noting that human data had been used in this way by EFSA for other compounds with a presumed linear dose-response relationship, such as lead.

1.78 The final EFSA opinion is now published.

EFSA public consultation on “Update of the risk assessment of mineral oil hydrocarbons (MOH) in food”

1.79 The EFSA were asked by the European Commission (EC) to assess any toxicity studies on mineral oil hydrocarbons (MOH), that had become available since the 2012 EFSA evaluation and to update their scientific opinion, if necessary. EFSA were also asked to update their exposure assessment and to update the risk characterisation, if necessary. The COT were asked to comment on the draft opinion.

1.80 The Committee noted that the datasets for mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH) differed significantly and hence the current opinion should really be considered as two different assessments, one for MOSH and one for MOAH.

1.81 Following the publication of the 2012 opinion, EFSA commissioned toxicology studies on MOSH, which were available for the current evaluation. The rat study provided additional data on the Fischer rat and hence allowed for a clear conclusion on strain sensitivity, which had previously been suggested but not confirmed. The study used to establish the Health Based Guidance Value (HBGV)

proposed in the EFSA opinion was a well-defined study, with the No Observed Adverse Effect Level (NOAEL) being at the highest dose tested. Overall, the Committee agreed with EFSA's approach to the assessment of MOSH.

1.82 Members also agreed with the overall approach taken by EFSA for the assessment of MOAH, utilising the BMDL10 for PAH8 in the absence of studies to define a reference point (RP) for 3- or more ring MOAH.

1.83 However, Members would have liked to have seen additional detail on the derivation of the uncertainty factors, in particular the application of an additional uncertainty factor of 6. While the Committee did not disagree with the use of the additional factor, the discussion and underlying reasoning was complicated, and a clearer definition/explanation would have been useful.

1.84 Overall, the Committee agreed that the 2023 EFSA draft opinion was a good compilation and discussion of the available data and agreed with EFSA's approach and conclusions.

1.85 Members noted that setting standards for MOH was difficult, especially as MOH was a mixture of compounds, often not well defined. Hence it was difficult to conclude on a representative chemical, and the assessment was further complicated by the fact that there was incidental exposure to other MOHs.

1.86 The Committee would have liked to have seen further details covered within EFSA's recommendations, especially with regard to the specifications of food grade MOH, and other sources of MOAH in food.

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

1.88 The final EFSA opinion is now published.