Meeting

Second draft interim position statement on bisphenol A

This is a paper for discussion.

This does not represent the views of the Committee and should not be cited.

Introduction

1. In April 2023, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) established a new tolerable daily intake (TDI) of 0.2 ng BPA/kg bw per day. Although this new TDI is higher than the initially proposed level of 0.04 ng/kg bw, mean and high level consumers for all age groups would exceed the new TDI by 2-3 orders of magnitude.

2. The COT discussed the draft EFSA opinion at their extraordinary meeting in February 2022 and provided comments on the public consultation. The final EFSA opinion and diverging opinions by the EMA and the BfR were discussed at the May 2023 COT meeting.

3. Attached at Annex A is the second draft interim position statement, following comments by the Committee in May. Additional text has been added to the second draft statement, expanding on the background/general information on BPA, the concerns raised by the COT on the selection of the endpoint by EFSA and recommendations of the COT on how to take the work forward to derive a UK tolerable daily intake.

Question on which the views of the Committee are sought

i. Do Members have any comments on the content and structure of the draft interim position paper?

ii. Do Members have any comments on the continued use of the current temporary TDI while the review of BPA is being undertaken?

iii. Does the Committee have any further comments?

Secretariat

September 2023

TOX/2023/45 Annex A

Introduction and background

1. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) reviewed the scientific basis and implications for risk management of the new EFSA tolerable daily intake (TDI) for bisphenol A (BPA).

2. BPA is authorised for use in food contact materials. It is used in rigid plastics such as reusable bottles, tableware and storage containers, as well as thermal printing in certain paper products and for protective linings of food and beverage cans and vats (EFSA, 2021). A specific migration limit of 0.05 mg/kg was set in the European Union (EU) and United Kingdom (UK), following the European Food Safety Authority's (EFSA) 2015 evaluation of BPA.

3. The temporary TDI (tTDI) established by EFSA in 2015 of 4 µg/kg body weight (bw)/day was based on increased mean relative kidney weight in animal studies and a human equivalent dose (HED). Based on the 2015 exposure assessment EFSA concluded that there was no health concern for any age group from dietary exposure and low health concern from aggregate (dietary and non-dietary) exposure. However, EFSA noted considerable uncertainties in the exposure estimate for non-dietary sources.

4. In 2016, EFSA received a mandate from the European Commission to re-evaluate the risk to public health related to the presence of BPA in foodstuffs. The re-evaluation should take into consideration data that became available since the last assessment and should seek to clarify the remaining uncertainties concerning the toxicological endpoints of BPA.

4. The COT discussed the draft EFSA opinion at an extraordinary meeting in February 2022 and submitted detailed comments to the EFSA public consultation. The final EFSA opinion was published in May 2023.

2023 EFSA evaluation

5. For the derivation of their new TDI, EFSA's Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) assessed the evidence from animal data and human observational studies and identified the immune system as the most sensitive endpoint to BPA. An increase in the percentage of TH17 cells in mice, cells which are critical for immune mechanisms and involved in inflammatory conditions, was considered as the most sensitive endpoint and hence the critical effect of BPA.

6. The new tolerable daily intake (TDI) of 0.2 ng BPA/kg bodyweight (bw) per day was based on a human equivalent dose (HED) of 8.2 ng/kg bw per day, converted from the lowest BMDL40 of an increase in the percentage of TH17 cells in mice. EFSA applied an overall uncertainty factor (UF) of 50, the default UF of 2.5 and 10 for interspecies toxicodynamic differences and intraspecies variability in toxicokinetics and toxicodynamics, respectively. No uncertainty factor was applied for inter species variability in toxicokinetics as this was already accounted for in the conversion to the HED. EFSA did however apply an additional UF of 2 based on the uncertainty analysis performed.

7. The new TDI is substantially lower than the previous level of 4 µg/kg bw and based on the exposure assessment performed by EFSA in 2015, mean and high-level consumers of all age groups could potentially exceed the new TDI by 2-3 orders of magnitude.

8. Both, the European Medical Agency (EMA) and the Bundesamt fuer Risikobewertung (BfR) provided comments to EFSA, highlighting their diverging views from EFSA, i.e., on the use of an intermediate endpoint for the derivation of a health-based guidance value (HBGV), the approach and timeframe applied for consideration of studies, and the risk assessment approach including the uncertainty analysis and clinical relevance/extrapolation from animals to humans and derivation of the HED. As the diverging views could not be resolved, EFSA and the EMA/BfR were obliged to present a joint document to the European Commission clarifying the contentious scientific issues and identifying relevant uncertainties in the data.

COT view

9. The final EFSA opinion and diverging views by the EMA and BfR were discussed by the COT at their May 2023 meeting. The COT noted that the

scientific issues raised by the EMA and BfR aligned with the concerns and comments highlighted by the COT during the public consultation and May meeting.

10. The Committee considered that there was a lack of transparency on how the evidence had been integrated to derive the point of departure (POD) for the derivation of a HBGV.

11. EFSA utilized a predetermined protocol which restricted their inclusion of studies and subsequent data evaluation to a specific time period. While the Committee acknowledged that due to its size, it would not be feasible to assess the full database on BPA, and other studies would likewise have uncertainties, there was a wider data set available for BPA, which should have been considered in the evaluation for the relevant endpoint selection but also the derivation of the human equivalent dose (HED) factor. The Committee further queried whether an intermediate endpoint would be sufficiently robust to derive a HBGV but specifically did not agree with EFSA's assessment that the increase in percentage of Th17 cells was a scientifically relevant and robust intermediate endpoint to be applied to the derivation of a new HBGV. Given the uncertainties over the endpoint a more robust weight of evidence approach and evidence integration should have been applied to a wider dataset to derive a more reliable and relevant endpoint on which to base the HBGV.

12. EFSA (2015) previously compared the temporary TDI (t-TDI) with exposure estimates and concluded that there was no health concern for any age group from dietary exposure and low health concern from aggregate exposure. In the current opinion EFSA was not explicitly asked to perform an exposure assessment and hence used the assessment from 2015, noting that the data used may not accurately reflect the current exposures to consumers. The COT agreed with the uncertainties in this approach and noted that work has been undertaken by industry to lower exposures to BPA and hence, the previous data may not be reflective of the current exposures.

Conclusions and next steps

13. While the Committee considered it possible that the TDI would need to be revised to account for new evidence and ensure it was sufficiently protective, on balance the weight of evidence did not support the conclusions drawn by EFSA , or a TDI as low as that derived by EFSA. The Committee will therefore undertake their own weight of evidence approach and perform a transparent data

integration, utilising the guidance on the synthesis of epidemiological and toxicological evidence (SETE), where applicable.

14. While the COT acknowledges that given the size of the database, this will not be a short undertaking, the work will aim at identifying key endpoints, gaps and uncertainties and suggest a way forward on a robust point of departure from which to derive a TDI.

COT position paper

September 2023