Minutes

# Final Minutes of the 4th February 2025 COT Meeting

**Meeting of the Committee at 10:00 on the 4th of February 2025 on Microsoft Teams.**

## Present

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| Chair: | Professor Alan Boobis | Committee on Toxicity |

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| | Dr Stella Cochrane | |
| Members: | Professor James Coulson | |
| | Professor Gary Hutchison | |
| | Professor Thorhallur Ingi Halldórsson | |
| | Dr Gunter Kuhnle - up to item 7. | |
| | Dr David Lovell | |
| | Professor Shirley Price (Deputy Chair) | |
| | Dr Mac Provan | |
| | Dr Michael Routledge | |
| | Dr Natalie Thatcher | |
| | Professor Mireille Toledano | Committee on Toxicity |
| | Professor Philippe Wilson | |
| | Professor Maged Younes Dr Steven Enoch | |
| | Professor Peter Barlow – except items 5 and 6. | |
| | Dr Meera Cush | |
| | Mr Gordon Burton | |
| | Dr Andreas Kolb | |
| | Mr Nick Richardson | |
| | Dr Simon Wilkinson (from Item 6 onwards) | |

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| Liaison Member | Professor Paul Haggarty (items 6) | Scientific Advisory Committee on Nutrition (SACN) |

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| (FSA) Secretariat: | Ms Cath Mulholland | |
| | Dr Alex Cooper | |
| | Mr Barry Maycock | |
| | Ms Claire Potter | |
| | Ms Chara Tsoulli | |
| | Dr Barbara Doerr | |
| | Dr Olivia Osborne | |
| | Ms Sabrina Thomas | |
| | Dr Gail Drummond | |
| | Ms Frederique Uy | |
| | Ms Jocelyn Frimpong-Manso | Food Standards Agency |
| | Ms Sophy Orphanos | |
| | Dr Gaetana Spedalieri | |
| | Mr Thomas Hornsby | |
| | Dr Emily Hudson | |
| | Dr Aaron Bradshaw | |
| | Ms Natasha Adams | |
| | Dr Katie Schulz | |
| | Ms Rachel Kerr | |
| | Mr James Metcalfe | |
| | Ms Yoana Petrova | |
| | Ms Alba Ureña Rusillo | |

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| UK HSA Secretariat: | Ms Britta Gadeberg | UK HSA Scientific Secretary |
| | Ms Sanyukta Pallavi | |
| Assessors | Mr Benjamin Harding – item 6 & 7 | Health and Safety Executive |
| Assessors | Ms Hannah Jones | Business, Energy and Industrial Strategy |
| Assessors | Mr Ian Martin | Environment Agency |
| Assessors | Ms Akosua Adjei | Medicines and Healthcare Products Regulatory Agency |
| Invited Experts | Dr Stuart Adams - Item 5 | FCM JEG |
| | Dr Sibylle Ermler- Item 5 | |
| Invited Experts | Mr Will Smith | FSA (ACNFP Secretariat) |
| FSA and officials from other Government Departments | Mr Vincent Greenwood | FSA |
| | Ms Helen Twyble - Items 6 & 7 | |
| | Ms Clare Mccartney-Collard – Item 7 | |
| | Dr Joseph Shavila - Item 6 | |
| | Mr Allan Shivembe - Item 5 | |
| | Ms Pamela Iheozor-Ejiofor | |
| UK HSA Officials | Ms Nive Raja | UK HSA |
| | Mr Stephen Robjohns | |

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# Announcements

1. The Chair welcomed Members and other attendees.

2. Members were informed that Dr David Gott, who recently retired from the Secretariat, was awarded an OBE in the New Year’s Honours list for services to toxicology. The Committee asked the Secretariat to pass on their congratulations to Dr Gott for this very well deserved recognition.

# Interests

3. The Chair reminded those attending the meeting to declare any commercial or other interests they might have in any of the agenda Items.

# Item 1: Apologies for absence

4. Apologies were received from COT Members Dr Cheryl Scudamore, Dr Alison Yeates, Dr Chris Morris and Dr Silvia Gratz, Science Council Liaison Tom Oliver HSE Assessor Minako Allen, and Ms Liz Lawton, HSE.

# Item 2: Draft minutes and reserved minutes of the 21st of October 2024 meeting. (TOX/MIN/2024/06)

5. The Committee reviewed the draft minutes and the reserved minutes of the 10th of December 2024 meeting (TOX/MIN/2024/07). It was noted that there were some minor typographical errors in the main minutes, which would be amended by the Secretariat.

6. Subject to the above amendments, the minutes and reserved minutes were accepted as an accurate record.

# Item 3: Matters arising

## Joint Expert Group (JEG) updates

### AEJEG

7. The most recent meeting of the main Additives, Enzymes and other Regulated Products Joint Expert Group (AEJEG) was held on 4th of December 2024 and several items were presented. These included an update paper and a third draft Committee Advice Document (CAD) on the application for the authorisation of blue microalgae extract (blue Galdieria extract) for use as a new food additive in the “colour” functional class (RP507). The AEJEG, with the support of a COT Member invited as a statistical expert, discussed a 90-day study which was part of the application. It was agreed that the Secretariat would present the CAD document to the AEJEG meeting in February for final review. A cover paper for the authorisation of 2,4-dimethyl-5-vinylthiazole [FL-no:15.005], 4-Methyl-5-vinylthiazole [FL-no:15.018] and 4,5-dimethyl-2-isobutyl-3-thiazoline [FL-no:

15.032] for their use as food flavourings was also considered.

8. The Secretariat explained that Committee Advice Documents (CADs) will be produced for those smoke flavouring primary products considered genotoxic *in vivo* by the AEJEG Smoke Flavouring Working Group (SFWG). Interim summaries will be produced for those smoke flavouring primary products not considered genotoxic *in vivo* by the AEJEG SFWG. CADs and interim summaries will be presented to COT Members in 2025, once cleared by the AEJEG SFWG.

9. The next main AEJEG meeting will be held on 11th of February 2025, with the next meeting of the SFWG being on 19th of February 2025.

10. The Secretariat is in the process of finalising the FSA/FSS safety advice for RP1457 (glycolipids), RP42 (nisin), and RP1245 (steviol glycosides) with a planned publication date of 27th March 2025.

**FCMJEG**

11. The last meeting of the Food Contact Materials JEG (FCMJEG) was held on 4th December 2024. The FCMJEG assessed a new application for a plastic additive (RP2263 – Agar Palmitate) and agreed to send a Request for Further Information (RFI) to the applicant. Following the FCM JEG meeting the Applicant has since notified the Secretariat that they may change the manufacturing process; should this be the case, the applicant would be advised to withdraw the present application and resubmit a new one.

12. The FCMJEG also discussed some amendments to the Committee Advice Document (CAD) for a plastic additive application (RP1702), which is due to be concluded at a future meeting. Currently there are 3 recycling process applications (RP1741, RP1862, RP1898) and 2 plastic additive applications (RP2147 and RP2263) under review. One plastic additive application is at the RFI stage (RP2147).

13. The next FCMJEG meeting is on 26th of February.

## Publications

14. Members were informed that the 2023 Annual report had been published on the COT website.

## Subgroups and working groups

**ACNFP/COT working group on CBD**

15. The last meeting of the joint WG took place on Wednesday 22nd January 2025 and discussed “Group C toxicological profiling”. These are products that contain between 2.5 and 67% CBD.

**PFAS Working Group**

16. A date for the next meeting of the PFAS working group has not yet been set. A request was made that an update on the work to date was provided to the working group following this meeting. The Secretariat would action this.

**Joint SACN COT working group on plant-based drinks.**

17. The next meeting of this group will take place at the end of February, where the WG will consider the revised report following the peer review consultation.

## EFSA public consultation on the update of the ‘Scientific opinion on the risks for human health related to the presence of perchlorate in food’

18. Professor Thorhallur Ingi Halldórsson declared an interest for this item since he is a member of EFSA’s working group on perchlorate. This was considered a personal specific interest and Prof Halldórsson was excluded from the discussion, though he was able to answer questions and provide clarification on the draft EFSA opinion. Dr Meera Cush noted that she had conducted a human health risk assessment for a tea manufacturer two years ago following a perchlorate contamination incident. However, although a personal, specific interest this was not considered to be a conflict as it represented only prior experience of assessing perchlorate, thus Dr Cush was not excluded from the discussion. No other interests were declared.

19. The Secretariat had not provided a cover paper for this item but had provided some summary text which had been circulated to Members prior to the meeting together with the link to the EFSA document.

20. EFSA began a public consultation on a draft opinion on the assessment of risk from perchlorate in food in January 2025. In the draft opinion, the Tolerable Daily Intake (TDI) had increased from 0.3 µg/kg bw per day to 1.4 µg/kg bw per day. Both the previous assessment (2014) and the reassessment (2025) based

their health-based guidance value (HBGV) on the same study, in which iodine uptake in the thyroid in healthy human volunteers had been assessed. However, differences in the modelling approach used to determine the benchmark dose (BMD) and the different uncertainty factors applied resulted in different HBGVs.

21. Members noted that no background or zero dose level data were available in the human study used by EFSA. Out of the three dose levels assessed, the lowest dose level was extrapolated as the zero dose level in order to apply the new Bayesian Benchmark Dose (BMD) methodology. According to EFSA's (2022) Guidance on the use of the BMD approach in risk assessment, "few practical examples of application of BMD modelling in the absence of non-exposed controls exist. The more widespread use of the BMD methodology may highlight the need to update this guidance in this respect." The Committee noted that they were not aware of any updates to this guidance.

22. Members agreed that the derivation of the BMDL was critical to the whole assessment, and it was unclear how EFSA had derived the BMDL05 of 7 µg/kg bw/day for perchlorate from the numbers described. Members also noted that a Benchmark Response (BMR) of 5% was selected by EFSA to represent an adverse effect at the population level. This is because individuals at the extreme ends of the distribution curve would show more (or less) than 5% inhibition of iodine uptake, respectively and hence would be at greater (or lesser) risk. Members discussed the application of an uncertainty factor to account for interindividual variation and noted that such factors are intended to account for population variation. Hence the approach used by EFSA (and others) might be overly conservative in such situations and this observation should be included in the comments submitted by the Members to EFSA.

23. A Member had attempted to reproduce EFSA's BMD modelling results using three (of nine) variables provided, which resulted in a BMDL05 of 9 µg/kg bw/day for perchlorate. This highlighted that subtle changes in the input can change the results, and thus Members argued that further work was required on this type of modelling.

24. The deadline for submitting comments to EFSA was 11th February and Members were asked to submit any additional comments to the Secretariat by 7th February 2025.

## Liquorice in the maternal diet

25. No Interests were declared.

26. At the Scientific Advisory Committee on Nutrition (SACN) Nutrition and Maternal Health Working Group (NMHWG) meeting held on 21st October 2024, SACN Members raised concern about the potential effects of excess liquorice, especially liquorice tea, in the maternal diet, as liquorice was sometimes consumed during pregnancy to relieve constipation. Therefore, the COT were asked to consider adding liquorice to the list of substances to review as part of the ongoing maternal diet work programme and potentially to review its effects in all populations.

27. The COT noted that there were numerous active chemical constituents in liquorice and further clarification was required on whether they were being asked to assess liquorice extract as a whole, or the individual chemical constituents.

28. It was noted that some of the chemical constituents present in liquorice had pharmacological activity and had been considered with a view to developing them as pharmaceuticals (e.g. carbenoxolone), resulting in a large amount of information potentially being available.

29. Members noted that the main adverse effect associated with high liquorice consumption was hypertension. Therefore, Members questioned whether the concern about liquorice was broader than the effects on the cardiovascular system.

30. Members noted that consumption of liquorice was particularly high in Scandinavian countries and those countries could be a source of useful information.

31. The Committee suggested that a scoping paper or survey might be necessary to identify common liquorice products, patterns of use, and where the products were obtained from. This information could form the basis of the review on liquorice.

32. The COT agreed that liquorice should be added to the list of items to be reviewed as part of the maternal diet programme.

## Abbreviated process for regulated products decision panel

33. Last year it was agreed that the FSA would periodically update the Scientific Advisory Committees (SACs) and Joint Expert Groups (JEGs) on those applications that have been assessed via the other regulators' opinion (ORO) or the abbreviated process (ABB) routes and have been internally assured through

the FSA Regulated Products Decision Panel.  The first of these updates was shared in September 2024 and a further update was provided to Members for information. Members were reminded that the update contained commercially sensitive and confidential information.

34. Members commented that if these applications had come through the Joint Expert Groups (JEG) and/or COT then additional questions about safety may have arisen, as some of the applications were similar to those assessed by the Committee route. The Committee suggested that safety assessments taken to the Decision Panel that are similar to CADs reviewed by the COT could be compared to evaluate whether the same questions are being raised and to streamline both processes.

# Item 4: Joint position paper from the Advisory Committee on Novel Foods and Processes ( ACNFP) & Committee on Toxicity (COT) on establishing a Safe Upper Limit for delta-9-tetrahydrocannabinol (Δ9-THC) and its precursor as contaminants of hemp-derived products and CBD novel foods Draft Statement (Reserved)

35. Professor Philippe Wilson declared that he was director of a company dealing with medical cannabis. It was agreed that he should not take part on the discussion of this item. Dr Stella Cochrane and Dr Natalie Thatcher had historic personal non-specific interests as their employers have had an interest in potentially developing products containing CBD; this did not preclude them from taking part in the discussion of this item. No other interests were declared.

36. To support the assessment of cannabidiol (CBD) novel foods the Joint Advisory Committee on Novel Foods and Processes (ACNFP) and COT Subgroup have developed a statement on a safe upper intake level for tetrahydrocannabinol (THC) as a contaminant of food. The statement summarises the position reached by the Subgroup and the evidence that underpins it. This view has been reflected in recent safety assessments for CBD novel foods. Members’ comments are sought with a view to seeking agreement to the joint

statement by the COT and the ACNFP.

37. The Committee reviewed the draft statement which is currently being treated as reserved. The final statement will be published in due course.

## Item 5: Draft Committee Advice Document on the recycled poly (ethylene terephthalate) decontamination process operated by Biffa Waste Services Limited for use in the manufacture of materials and articles in contact with food RP 1862 (Reserved)

38. No interests were declared.

39. Dr Stuart Adams and Dr Sibylle Ermler from the Joint Expert Group on Food Contact Materials (FCMJEG) were in attendance for this item.

40. The FCMJEG had been requested to provide an assessment on the recycled poly(ethylene terephthalate) decontamination process operated by an Applicant for use in the manufacture of materials and articles in contact with food.

41. This item is currently being treated as reserved, as the data are commercially confidential.

42. Members reviewed and commented on the draft Committee Advice Document.

## Item 6: Mercury in the maternal diet – TOX/2025/03

43. No interests were declared.

44. In 2020 the COT considered a prioritisation paper on substances to be considered for risk assessment as part of the COT’s current programme of work assessing risks from the maternal diet, which feeds into the Scientific Advisory Committee on Nutrition’s (SACN) review of nutrition and maternal health, focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after

delivery. Following discussion of the prioritisation paper the Committee decided that each of the heavy metals (lead, mercury, cadmium, and arsenic) should be considered in separate papers. This discussion paper focuses on the risks posed to maternal health (including that of the embryo/fetus) by mercury in the diet and the environment.

45. Mercury in the diet occurs as either inorganic mercury salts or organic mercury compounds, the latter being the more toxic form. Methylmercury (MeHg) is the most common form in the food chain. After oral intake in humans, MeHg is more extensively and rapidly absorbed than inorganic mercury, being able to readily cross the placental, blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in the fetus and brain. The main adverse effect associated with MeHg exposure is central and peripheral neurotoxicity. Therefore, due to the ability of MeHg to cross barriers, exposure during embryonic neurodevelopment and in young children is of high concern and pregnant and breastfeeding women are sensitive sub-populations. The potential risk of MeHg in the diets of infants and children has previously been assessed by the COT in 2018, where the Committee agreed that the risk to health at current exposure levels was low.

46. The European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) have both published risk assessments on exposure to MeHg and inorganic mercury in food. In 2003 JECFA established a Tolerable Weekly Intake (TWI) for MeHg of 1.6 µg/kg bw based on epidemiology studies from the Seychelles and Faroe Islands. In 2011 JECFA established a provisional TWI of 4 µg/kg bw for inorganic mercury, predominantly based on a National Toxicology Program (NTP) rat bioassay study (1993). EFSA reassessed these Health-Based Guidance Values in 2012 and established the same TWI for inorganic mercury, based on the same evidence as JECFA. A lower TWI for MeHg, of 1.3 µg/kg bw, was established due to the availability of new information on cofounding beneficial factors in fish on the associations between prenatal MeHg exposures and neurodevelopmental endpoints in the critical epidemiology studies.

47. Separate and aggregate estimates of exposure to mercury from food, water, soil and air had been calculated and were all below the EFSA TWIs for MeHg and inorganic mercury.

48. The Committee noted that MeHg was a known toxicant, which could cross the placenta, and could have an adverse impact on the central and peripheral nervous system. Inorganic mercury was of less concern to the developing fetus due to its low absorption and inability to cross placental or

blood-brain barriers. Exposure to MeHg via breast milk was dependent on maternal exposure but data in the literature suggested that the concentrations in breast milk were generally low. Members noted that there were some examples of a direct effect on fetal growth and the size of the baby.

49. The Committee concluded that based on the current exposure estimates, there was no concern when these were compared to the EFSA TWIs, which were protective of this sub-population. The epidemiology data, which considered maternal exposure and assessed post-partum effects, did not indicate any concerns that the current exposure to MeHg was a health concern.

50. Members noted that inorganic mercury could not be disentangled from MeHg in the exposure data; although this was alluded to in the discussion paper, it should be strengthened in the final statement. However, as inorganic mercury would be present at low levels, it was safe to assume that most of the exposure via the diet is in the MeHg form.

51. Members suggested that mercury entering the hair follicle should be discussed separately from the placenta and blood-brain barrier as although the former was important from a biomonitoring perspective, there were no toxicodynamic implications.

52. Members sought clarity on the kinetics of MeHg with respect to its distribution across tissues, the nature of the carrier(s) of MeHg, including a possible role of metallothionein, and whether measurements of MeHg in blood were of ‘bound’ or ‘free’. The Committee asked for the discussion on distribution to be simplified and checked for consistency. Members also noted questions regarding the solubility and storage of mercury in fat and how this might influence exposure during pregnancy.

53. Members discussed the current literature on selenium and evidence of its protection against MeHg toxicity. Limited research suggested selenium may detoxify mercury by sequestration or by other protective modes of action such as antioxidant effects. However, the Committee concluded that the current field of research was not conclusive as to the ability of selenium to ameliorate MeHg toxicity.

54. The Committee requested that the current Government advice on foods to avoid in pregnancy should be reiterated. Pregnant women were currently advised to avoid eating more than 2 portions of oily fish a week and no more than 2 tuna steaks (about 140 g cooked or 170 g raw). Shark, swordfish, marlin, raw

shellfish and uncooked cold-smoked or cured fish should also be avoided by pregnant women and women trying to get pregnant. It was noted that this advice also protected against potential dioxin exposure and microbiological hazards as well as potential mercury exposure. Members noted that if pregnant women and women trying to get pregnant were following Government advice the exposure assessment was highly conservative as fish and seafood were the major sources of MeHg exposure in the diet.

55. Members requested that the potential exposure to mercury through nutritional supplements such as cod liver oil should also be investigated and possibly included in the exposure assessment if levels of mercury were significant.

56. Members suggested some additional minor editorial changes to the paper for inclusion in the final statement.

## Item 7: Deriving a health-based guidance value for antimony to support development of UK Drinking Water Standards – further information – TOX/2025/04

57. No interests were declared.

58. The UK Health Security Agency, which advises the Drinking Water Inspectorate (DWI) on the health risks of chemicals in drinking water, requested advice from the COT on an appropriate health-based guidance value (HBGV) for antimony. This topic was initially considered at the COT meeting on 21st of October 2024 (paper TOX/2024/38). At that meeting, the Committee considered a 90-day rat drinking water toxicity study on antimony potassium tartrate by Poon et al. (Food and Chemical Toxicology, 36, 21-35, 1998). The World Health Organization, the US Agency for Toxic Substances and Disease Registry and Health Canada had all used this study to establish a HBGV, but these were all different, with the difference being due primarily to variations in the interpretation of the study findings, particularly in the identification of the No Observed Adverse Effect Level (NOAEL). At the October 2024 meeting, the COT identified a NOAEL of 6,000 µg Sb/kg bw/day for the Poon et al. (1998) study but requested further information on other studies in which the authors had reported lower points of departure, so that the Committee could identify the most appropriate study and endpoint to select for the critical effect.

59. The paper presented at the current meeting provided additional evidence relating to the toxicity of antimony, including reproductive and developmental toxicity data, and information on oxidation states, solubility, and bioavailability of different antimony compounds.

60. With respect to the developmental studies, the COT noted that the baseline maternal body weight in the study by Rossi et al. (Teratogenesis, Carcinogenesis and Mutagenesis, 7, 491-496. 1987) at gestation day 0 (GD0), i.e. prior to treatment, was approximately 7% higher in the controls than in the groups treated with antimony trichloride. Consequently, the observed 8–10% reduction in maternal body weight at gestation day 20 (GD20) used as the basis for the maternal Lowest Observed Adverse Effect Level (LOAEL) was considered a relatively small change, given the pre-existing baseline differences and not of toxicological significance. It was noted that in the study of Poon et al (1998) exposure to up to 50 x the dose of potassium antimony tartrate for 90 days had no effect on body weight, albeit the rats were not pregnant. The Committee further observed that while decreased pup body weight was reported in the Rossi et al. (1987) study in the high dose group, the investigation by Angrisani et al. (Current Therapeutic Research, 43, 153-159, 1988) involving antimony exposure found no significant changes in pup body weight when exposure was limited to the postnatal period. With the lower maternal body weights in the treated groups reported in the Rossi et al. (1987) study, it was suggested that the observed reduction in pup body weight could be secondary to maternal differences rather than a direct effect of antimony on pups.

61. The Committee raised concerns regarding the reliability of several older studies that had been summarised in the discussion paper, as access to their data was limited, and their interpretation was challenging. The overall quality of these studies remained questionable, presenting a significant limitation.

62. The NTP intraperitoneal (i.p.) study summary indicated that body weight effects were observed only at the highest dose (24,000 µg/kg bw/day or 9,600 µg Sb/kg bw/day), which was higher than the identified NOAEL of 6,000 µg Sb/kg bw/day from the Poon et al. (1998) study. This provided further reassurance on discounting the lower LOAEL relating to maternal body weight reported in the Rossi et al. (1987) study.

63. The Committee noted that WHO, ATSDR and Health Canada had all used the Poon et al. (1998) study to identify a point of departure. It was recognised that ATSDR had also considered the Rossi et al. (1987) and Angrisani et al. (1998) studies, in addition to that of Poon et al. (1998), in selecting the

critical NOAEL to derive its intermediate oral Minimal Risk Level (MRL). Due to uncertainties, ATSDR had discounted the Angrisani et al. (1998) paper and overall, ATSDR selected a critical NOAEL of 60 µg Sb/kg bw/day from Poon et al. (1998), which was lower than the NOAEL of 70 µg Sb/kg bw/day reported by Rossi et al. (1987). Members noted that WHO had cited the Rossi et al. (1987) study in its review but did not provide a comprehensive discussion of its findings.

64. The Committee also highlighted that the pentavalent form of antimony, which is predominant in drinking water, exhibited lower toxicity compared to the trivalent form. Since Poon et al. (1998) utilized the trivalent form (antimony potassium tartrate) in their study, the NOAEL of 6,000 µg Sb/kg bw/day was considered a sufficiently conservative estimate.

65. Overall, the COT concluded that the NOAEL of 6,000 µg Sb/kg bw/day, from the Poon et al. (1998) study based on decreased body weight gain and reduced food and water consumption in adult rats, was the appropriate point of departure to use as the basis of a HBGV for antimony.

66. The Committee recommended an uncertainty factor (UF) of 300, allowing 10 for interspecies differences, 10 for intraspecies variation, and 3 for subchronic to chronic extrapolation. This would result in a tolerable daily intake (TDI) of 20 µg Sb/kg bw/day as a HBGV.

# Item 8: Request for comment on EFSA’s Public consultation on the EFSA Panel on Food Additive and Flavourings (FAF) ‘Draft guidance on the preparation of an application for authorisation of a food additive submitted under 4 Regulation (EC) No 1331/2008 – TOX/2025/05

67. No interests were declared.

68. EFSA had launched a public consultation on their draft guidance on the preparation of an application for authorisation of a food additive submitted under Regulation (EC) No 1331/2008 on 18$^{th}$ of December 2024. The COT was requested to provide comments on this draft guidance for submission to the consultation.

69. The Additives and Enzymes and other Regulated Products Joint Expert Group (AEJEG) had commented on the draft guidance and these comments would be pooled with those of COT. Members noted that the AEJEG had provided a number of comments and a detailed review of the technical aspects of the guidance.

70. The COT commented that the lack of requirement for acute toxicity studies was not consistent with the draft “Scientific Opinion on Current Practice, Challenges, and Future Opportunities in the Safety Assessment of Newly Expressed Proteins in Genetically Modified Plants” which was currently open for consultation or with their novel foods guidance. The COT noted that consistency and alignment between different pieces of guidance would be beneficial, but not requiring acute toxicity data was a welcome change.

71. Members noted that a provision for the assessment of safety for the environment had been included in the draft. A large dataset was required within this guidance, which included much vertebrate testing; Members considered this approach had not reflected the potential use of new approach methodologies.

72. The COT noted that EFSA had not reconsidered the use of the 2-year bio-assay study for hazard assessment to evaluate carcinogenicity. The COT noted this was no longer considered a reliable or effective approach. Members stated that a more creative strategy could have been proposed for assessing the potential carcinogenicity of food additives.

73. The COT noted that there were instances in the guidance where EFSA had commented that regulatory science was not sufficiently mature to allow an assessment of risk, assessment of effects on the microbiome being given as an example. However, no guidance was provided to Applicants on the implications of this on preparing an application; whether products with potential concerns could not be proven safe as there were no suitable methods, or whether potential concerns would not be taken into account unless there was specific data suggesting that this was the case.

74. The inclusion of the gut microbiome as a topic within the guidance was welcomed by Members. It was noted that there are no currently agreed methods for assessing the overall impact on the microbiome. However, Members stated that it would be important that EFSA’s approach to addressing concerns about possible effects on the microbiome was consistent, as previously some additives have been blocked due to the absence of such data, while other, similar, ones had received positive opinions. It was noted that this would also be important for any

UK approach. EFSA's 2024 "Roadmap for the integration of gastro-intestinal (GI) tract microbiomes (human and domestic animal) in risk assessments under EFSA 's remit" was noted.

75. Members were reminded that any additional comments should be sent to the Secretariat for inclusion into the submission to EFSA's public consultation by 14th February.

## Item 9: EFSA Draft Guidance for Public Consultation: Draft guidance document on the submission of data for the evaluation of the safety and efficacy of substances for the removal of microbial surface contamination of foods of animal origin intended for human consumption. Request for comments. TOX/2025/08

76. No Interests were declared.

77. EFSA discussed the possible update of the document 'Guidance on the evaluation of the safety and efficacy of substances for the removal of microbial surface contamination of foods of animal origin intended for human consumption' at the 39th Plenary meeting of the EFSA Panel on Food Contact Materials, Enzymes and Processing aids (CEP Panel). The purpose of the update was to provide more/further detail on the data and information that should be provided by an applicant to EFSA.

78. During the public consultation process the COT has an opportunity to provide comment on the draft guidance. Particular attention was drawn to section 4 of the guidance document, which describes the requirements for toxicological testing.

79. Members were invited to comment on the guidance, and also to advise on whether they agree with EFSA's approach for the requirements for the toxicological assessment. Members were informed that due to the short deadline, it would not be possible to take any additional comments following the meeting. It was noted that the draft guidance had been shared with the FCMJEG who had no

comments.

80. The Committee noted that the toxicology testing section relied on the recently prepared additives guidance (discussed under the previous item), and that any comments would apply to both. Members noted that concerns with respect to allergy were addressed using the novel food guidance which Members felt was a sensible approach.

81. Members noted that an environmental risk assessment was required as part of this guidance and that it also contained discussion of anti-microbial resistance.

# Item 10: Annual Report update and Horizon Scanning – TOX/2025/05

# COT draft Annual Report

82. Annex A of TOX/2025/05 contained the draft text of the COT section of the 2024 Annual report for the Committees on Toxicity, Carcinogenicity, and Mutagenicity of Chemicals in Food, Consumer Products and the Environment.

83. Members were invited to comment on the report and to consider how the COT had performed during 2024 against the Good Practice Guidelines for Committees advising the FSA; These were also annexed to the paper.

84. Members considered the different aspects of the Good Practice guidelines and agreed that in general, the Committee had performed well against them.

85. It was agreed that the different sections of the report would be divided up between Members to review the report in its entirety. Members were advised to send any comments or additional questions to the Secretariat.

86. Members suggested that the annual report could be a useful mechanism to publicise the work of the COT as a form of public engagement outreach. This could be done via the British Toxicology Society, for example.

87. Members were reminded to ensure their declarations for the register of interests were up to date.

## Update on actions taken subsequent to the Committee’s advice

88. Paper TOX/2025/06 provided Members with an update on how their advice has been used over the year. It was circulated largely for information and Members were asked to send in any questions or comments to the Secretariat. The Committee noted that the paper was very useful to capture the quantity and breadth of the work conducted by the Committee.

## Annual COT Horizon Scanning

89. Paper TOX/2025/06 introduced the annual COT horizon scanning session, reviewing all work anticipated for the year; this included both new and ongoing topics.

90. The Committee discussion focused on communication of the work they had undertaken and subsequently the advice taken. The COT considered their work to be both ‘reactive’ and ‘proactive’ which was consistent with their terms of reference, but the large majority of their work was reactive.

91. Members discussed whether the Committee needed to strike a better balance between the work they did in response to questions from FSA and other government departments and agencies, and topics where there was considerable consumer or media concern, justified or not, even if it was just for the Committee to comment that the issue was of no scientific concern or where there were too few data to reach any meaningful conclusion.

92. Members proposed a range of potential topics that could be considered; these included fermented foods, lab grown meat, food allergies and intolerances, future trade issues, and New Approach Methodologies (NAMs) for reproductive and developmental toxicity testing (DART). Members were informed that the FSA had begun a “regulatory sandbox” to assess cell cultivated proteins (lab grown meat)

93. The Committee agreed that Artificial Intelligence (AI) would be a suitable topic for the next COT Annual Workshop. It was intended that the proposed workshop be a first step towards reviewing the state of the art of AI technologies relevant to chemical risk assessment as well as discussing the opportunities and the challenges associated with the application of AI in chemical safety assessment. The next steps would be a proposal submitted to Members

about the content, structure, and format of the workshop.

94. Members were reminded that they could send any suggestions for subjects that might be considered by the COT to the Secretariat at any time.

95. Members were content with the current skills balance of the Committee.

## Item 11: Update on the work of other FSA Scientific Advisory Committees - for information

96. This paper was circulated for information, but Members could contact the Secretariat if they had any questions.

## Item 12: Any other business

97. There was no other business.

## Date of next meeting

98. The next meeting of the Committee will be held on the 26th of March 2025 at Clive House, London and via Microsoft Teams.

**Secretariat**

**February 2025**