Minutes

Final Minutes of the 10th December 2024 COT Meeting

Meeting of the Committee at 10:00 on the 10th of December 2024 on Microsoft Teams.

Present

Chair:	Professor Shirley Price (Deputy Chair)	Committee on Toxicity

Members:	Dr Stella Cochrane	
	Professor James Coulson	
	Professor Gary Hutchison	
	Professor Thorhallur Ingi Halldórsson	
	Dr David Lovell	
	Professor Shirley Price	
	Dr Mac Provan (Until Item 7)	
	Dr Michael Routledge	
	Dr Cheryl Scudamore	
	Dr Natalie Thatcher	
	Professor Mireille Toledano	Committee on Toxicity
	Professor Philippe Wilson	
	Dr Steven Enoch	
	Professor Peter Barlow	
	Dr Chris Morris	
	Dr Meera Cush	
	Mr Gordon Burton	
	Dr Andreas Kolb	
	Dr Alison Yeates (not present for items 6 and 7)	
	Mr Nick Richardson	
	Dr Simon Wilkinson	

Liaison Member	Professor Paul Haggarty (items 6, 7, and 8)	Scientific Advisory Committee on Nutrition (SACN)

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

UK HSA Secretariat:	Ms Britta Gadeberg Ms Sanyukta Pallavi	UK HSA Scientific Secretary
Assessors	Ms Rachel Elsom Ms Susannah Brown	OHID (Office of Health Improvement and Disparities)
Assessor	Dr Ovnair Sepai (until item 10)	UK Health Security Agency
Assessor	Ms Krystle Boss	Food Standards Scotland (FSS)
Assessor	Mr Leon Jackson	DEFRA
FSA and officials from other Government Departments	Mr Adam Hardgrave	FSA
FSA and officials from other Government Departments	Ms Catherine Hardy	Food Standards Northern Ireland
FSA and other officials	Ms Lucy Smythe	Food Standards Scotland

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Announcements

1. The Chair welcomed Members and other attendees.

Interests

2. 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

3. Apologies were received from COT Chair Prof Alan Boobis, COT Members Professors Gunter Kuhnle and Maged Younes and Dr Silvia Gratz. Apologies were also received from FCM JEG Member Dr Emma Bradley, Science Council Liaison Ms Jackie Healing and Ms Frederique Uy and Ms Tahmina Khan of the Secretariat. Apologies were also received from Mr Ian Martin (Environment Agency Assessor), Ms Frances Hill (OPSS/Department of Trade Assessor), Ms Louise Dearsly (HSE Assessor) and Ms Akosua Adjei (MHRA Assessor).

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

4. The Committee reviewed the draft minutes and the reserved minutes of the 21st of October 2024 meeting (TOX/MIN/2024/06). The minutes and reserved minutes were accepted as an accurate record.

Item 3: Matters arising

Joint Expert Group (JEG) updates AEJEG

5. The most recent meeting of the main Additives, Enzymes and other Regulated Products. Joint Expert Group (AEJEG) was held on the 4th of December and a number of 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 the final review. A cover paper for the authorisation 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 a food flavouring was also considered.

6. The AEJEG smoke flavourings working group (SFWG) met on 9th of December to continue with the last Phase 3 assessment on RP1613.

7. The next main AEJEG meeting will be held on 11th of February 2025, with the next meetings of the SFWG being at the end of February 2025, where Members will be asked to finalise the CADs and Summary documents concluding

on genotoxicity.

FCMJEG

8. The last meeting of the Food Contact Materials JEG (FCMJEG) was held on 4th December. 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. 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.

9. Currently there are 3 recycling process applications (RP1741, RP1862, RP1898) and 2 plastic additive applications under review (RP2147 and RP2263). One plastic additive application is in the RFI stage (RP2147).

10. Three recycling process applications have been concluded and the final documents are being drafted (RP45, RP53 and RP94).

Publications

11. The COT statement on green tea catechins has been published on the COT website (Statement on green tea catechins) and it is anticipated that a statement on turmeric will be published very shortly.

12. The 2023 Annual report has been significantly delayed for a variety of reasons but should be published before the end of the year.

Subgroups and working groups

ACNFP/COT Working Group on Cannabidiol (CBD)

13. The last meeting of this Working Group took place on 20th of November 2024 and discussed “Introduction to Group C”. These are CBD products which contain between 2.5 and 67% CBD. The next meeting of the WG will be on 22nd of January 2025.

Per and polyfluoro alkyl substances (PFAS) Working Group

14. A date for the next meeting of the PFAS sub-group has not yet been set.

Joint SACN COT Working Group on plant-based drinks

15. The joint WG met on 5th of November 2024 to review the responses to the peer review consultation of the draft report.

16. The WG agreed that there would be no significant reworking of any of the analyses but there would be a focus on clarifying wording. It is hoped that the report can be finalised in the Spring with a view to publication before the summer recess.

SAC Recruitment

17. The recruitment for a COT Chair and COT Members and Associate Members has now been completed and it is hoped that the appointments will be made in February 2025.

Item 4: Authorisation of the substance Glycolipids (E 246) (Nagardo, AM-1) for use as a new food additive (RP1457) (Reserved) TOX/2024/41

18. Dr Meera Cush declared a personal non-specific interest since the application was submitted by LANXESS Deutschland GmbH who is a client she works for directly but in relation to for non-food registrations in South Korea. This did not preclude her taking part in the discussion of this item.

19. A confidential AEJEG Committee Advice Document (CAD) for the authorisation of the substance Glycolipids (E 246) also known as AM-1, for use as a new food additive with a proposed use in beverages, was presented to the COT for comment.

20. The item is currently being treated as reserved whilst policy is developed. The minutes will be published once confidentiality agreements have been finalised.

21. Members reviewed and commented on the document.

Item 5: Extension of use of nisin (E 234) to a new food category “egg analogues” (RP42). (Reserved) TOX/2024/42

22. No interests were declared.

23. A confidential AEJEG Committee Advice Document on the Extension of use of nisin (E 234) to a new food category “egg analogues” was presented to the COT.

24. The item is currently being treated as reserved whilst policy is developed. The minutes will be published once confidentiality agreements have been finalised.

25. Members reviewed and commented on the document.

Item 6: Echinacea in the maternal diet TOX/2024/43

26. No interests were declared.

27. In 2020, as part of their ongoing programme of work assessing risks from the maternal diet, the COT considered a scoping paper which reviewed commonly used herbal supplements during pregnancy. This work feeds into the Scientific Advisory Committee on Nutrition’s (SACN) review of nutrition and maternal health, which is focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery. Following their review of the scoping paper, the COT agreed that Echinacea required further investigation with main areas of concern including general toxicity to the mother, effects on the development of the fetus or embryo, and possible interactions with drugs.

28. There are three Echinacea species used medicinally or in supplements with various products being available on the market. These products contain single or combinations of Echinacea species, different parts of the plants, or their extracts. Some herbal products containing Echinacea have a Traditional Herbal Registration (THR) license from the Medicine and Healthcare Products Regulatory Agency (MHRA) based on traditional use for the relief of common cold symptoms. In addition to products with herbal medicinal licenses, there is a range of foods and food supplements containing Echinacea and they are the focus of the paper presented.

29. Data from surveys on the use of herbal medicines during pregnancy suggests that pregnant women use Echinacea for the treatment and prevention of cold/flu and immune system support. However, there is a lot of uncertainty around the safety of using Echinacea products during pregnancy and/or lactation

due to the limited data available from *in vitro*, *in vivo* and clinical studies. The MHRA and the European Medicines Agency (EMA) do not recommend the use of medicinally licensed Echinacea products for pregnant or lactating women due to the lack of sufficient safety data.

30. Some Members asked about the efficacy of Echinacea in the treatment and prevention of the common cold and hence raised the issue of a risk benefit analysis. However, this was beyond the remit of the FSA and that the discussion paper only considered food supplements, not the herbal products with THR overseen by the MHRA. It was asked whether the Yellow Card Adverse Drug Reaction Scheme could be a source of information as this would capture adverse drug reactions to Echinacea products with a THR license. While these reports were forwarded to the FSA when the products were classified as food supplements, the Secretariat were not aware of any reports for Echinacea.

31. The first aim of the discussion paper on Echinacea in the maternal diet was to seek the views of the Committee on the risks to maternal health associated with consumption of Echinacea in foods and food supplements during pregnancy. The second aim was to ask the Committee whether a point of departure (POD) could be derived for use in risk assessments on the basis of the available data.

32. Committee Members recommended clearer structuring of the data, including tables and summaries to make the complex and conflicting findings easier to assess. This was particularly relevant for the section on the immunomodulatory effects of Echinacea, which contained information on a variety of effects exerted by Echinacea on different immune system cell types and subsequent cytokine production. The Members also suggested that the anti-inflammatory and immunomodulatory effects of Echinacea should be considered within the same section of the dossier rather than as separate sections.

33. Members requested that the range of women reporting the use of Echinacea during pregnancy should be corrected in the paper from 4.3-9.2% to 0.5-9.2% in order to take into account the data from the study by Heitmann et al. (2016). In addition, it was noted that one of the studies reporting the percentage of women using Echinacea (Holst et al., 2011) during pregnancy was conducted between the months of November and February, which could lead to an overestimation due to increased incidence of cold and flu infections during the winter months.

34. Members noted that many of the food supplements suggested only short-term use of Echinacea and considered that this should be more clearly emphasised within the exposure section of the paper. The transient exposure made it difficult to determine the percentage of women using Echinacea during the different stages of pregnancy or lactation and what the implications of extrapolating from different types of studies would be.

35. Members sought clarity on the reproductive and developmental window covered when considering the safety of Echinacea in the maternal diet. As part of this discussion, it was emphasised that the maternal diet exposure window should focus on conception, maternal development, sustaining of the fetus, and post-partum exposure to Echinacea via lactation. The Committee noted the challenges in separating exposure via the maternal diet from other factors that could influence maternal health.

36. It was considered that the paper would benefit from a clearer separation of the reproductive and developmental data. Members suggested that this could be done in the form of a table or schematic summary of the reproductive and developmental endpoints covered by the available animal and human studies. Members agreed that this would draw the attention to the data gaps for the different points of the reproductive and developmental cycle. Members added that identifying these data gaps was particularly important given the recommended short-term use of Echinacea leading to a transient exposure window during the different parts of the reproductive and developmental cycle.

37. The Committee Members agreed there was lack of high-quality data on the reproductive endpoints from both animal and human studies. A potential data gap identified by Members was the absence of studies looking at the placenta and the maintenance of pregnancy. It was noted that whilst the study by Barcz et al. (2007) considered fetal angiogenic effects, it did not focus on the placenta.

38. Members discussed the *in vivo* mouse study by Chow et al. (2006) and the epidemiological study by Gallo et al. (2000) in more detail. They pointed out that the conclusion reached by Chow et al. (2006) that Echinacea could lead to miscarriages in early pregnancy was not convincing as the authors used a mouse strain (DBA) associated with small litter sizes and noted the authors did not provide any range/standard deviation with their results on fetal loss. Members commented that the sample size (n=206) in the study by Gallo et al. (2000) would not give sufficient statistical power to detect the birth defects and malformations studied. Members requested that the Secretariat should provide more information on the statistical tests used by Gallo et al. (2000), if this was

stated in the study methodology.

39. Members commented that the limited human studies on the use of Echinacea during pregnancy focussed on observations that could be detected at birth and did not consider any longer-term effects such as epigenetic changes. It was suggested that that this should be added as a caveat in the risk characterisation section.

40. Members discussed whether the study by Ondrizek et al. (1999), looking at the effects of Echinacea on sperm motility, should be removed from the paper as it focuses on a male reproductive end point, and this was outside of the maternal diet remit. The Secretariat confirmed that occasionally male reproductive end points were included when this was relevant to the mechanism of action. It was agreed that the study should be placed in an annex, so it was available for further information if needed.

41. The Committee considered the risk to maternal health from Echinacea exposure during pregnancy to be low but highlighted that there was insufficient information to enable a robust risk assessment. In terms of deriving a point of departure for use in risk assessments, it was stated that the 13-week repeated oral toxicity rat study by Jeong et al. (2024) could serve as a starting point, but this would require further evaluation and careful consideration of the endpoints. Members agreed that the point of departure might be difficult to derive due to complexity in terms of the range of preparations, extracts, doses assessed and the lack of sufficient, high-quality data to determine clear safety risks. It was also acknowledged that individuals with atopic disease or autoimmune disorders will be at higher risk from exposure to Echinacea products and this should be taken into account for the risk assessment.

42. Members made some comments on typographical errors and minor inaccuracies within the paper to be corrected by the Secretariat. The Committee confirmed that the paper would return as a first draft statement with the requested amendments. It was suggested that the statement should make a clear distinction between the conclusions reached by the individual studies and the COT conclusions.

Item 7: Third Draft Statement on the Safety of Ginger Supplement Use in Pregnancy TOX/2024/44

43. No interests were declared.

44. As part of the current programme of work on the maternal diet, the Committee is evaluating the use of dietary supplements during pregnancy. Following an initial review, the COT agreed ginger required further investigation, noting that human, animal, and *in vitro* data were available.

45. In May 2021, the Committee considered the potential effects of ginger and ginger supplements during pregnancy and lactation. Paper TOX/2021/26 reviewed the available data on toxicity to the mother, effects on the development of the fetus or embryo, and possible interactions with drugs as well as data on potential exposure.

46. Overall, it was concluded that there were limited data. The human data presented were not strongly indicative of any toxicological concern but there were some indications of possible adverse effects. The Committee also noted that in reviewing the data there were many uncertainties which should be considered in the conclusions. Ginger did not appear to be systemically toxic but did appear to have reprotoxic effects at high supplemental doses in laboratory animals.

47. Members noted that although the different ginger extracts were not comparable, they did appear to exhibit some biological activity in the early stages of pregnancy. It was reiterated that there was no indication of general systemic toxicity from the use of ginger.

48. A draft statement was considered in July 2022, drawing on the information provided in the previous discussion papers to form an overall conclusion on the safety of the use of ginger and in particular ginger supplements in the maternal diet. A second draft statement was considered in December 2022 which included additional studies identified by the COT to further inform the available database with regard to the possible influence of ginger components on cyclooxygenase (COX) and prostaglandin activity.

49. In the current statement, presented in paper TOX/2024/44, studies published since the second draft statement was considered by the COT have been added. The studies have also been split into ginger as used for culinary purposes and extracts/concentrated preparations of ginger. A summary of all of the studies considered was tabulated in Annex B for reference.

50. Annex D contained information on red ginger which is used in traditional medicine in Asia. Health claims relating to red ginger reference the benefits of consuming red ginger for emesis and pain during, and following, pregnancy. The consumption of red ginger in the diet is not common due to the difference in taste when compared with common ginger. There is limited evidence to suggest that red ginger is commonly purchased or consumed in the UK, but it is available for purchase online.

51. The Committee were asked to review the statement and the additional information to ensure the conclusions still represented the data and the views of the Committee.

52. Members made a number of minor editorial suggestions and requested that the wording describing the NHS and NICE advice on ginger to be included. They also questioned why the expert panel for cosmetic ingredient safety had considered orally dosed studies using ginger. This was confirmed as normal practise, as they needed to consider potential systemic toxicity and would be made clearer in the revised statement.

53. It was noted that the statement lacked information regarding the placenta and the ability of the constituents of ginger to cross the placental barrier. It was requested that the Secretariat check if there was information on this which could be added to the statement. If no data were available, then it should be identified as a data gap.

54. The Committee argued that the number of study participants should be included where applicable to aid the comparison of different studies.

55. When considering the conclusions the Committee considered that the text was confusing and the effects on animals and humans should be more clearly separated and described, and it should be stated that there is not a concern for pregnant women who consume ginger at levels found in the diet.

56. The Committee discussed the statement regarding the consumption data used for the exposure assessment being for women of childbearing age rather than pregnant women; this was included because pregnant women were usually excluded from dietary surveys, so there was little specific exposure data for them. It was noted a study conducted at Southampton University had concluded that there were limited differences in women’s diets prior to pregnancy compared to when they were pregnant. This study could be cited to add strength to the exposure calculations and conclusions.

57. The Committee discussed the information provided on red ginger. It was noted by Members that there were some differences between the two forms of ginger which were well characterised, but that currently red ginger was not widely available on the UK market. Where beneficial claims were quoted, it needed to be noted who had made the claims.

58. Overall, the Committee considered that the data on red ginger were limited and the section on red ginger should remain as an annex to the statement. Where it was stated that red ginger had relatively increased toxicity compared to common ginger, this should be expanded to include the specific end points.

59. It was agreed that the statement could be cleared by Chair's action.

Item 8: Discussion paper on the effects of calcidiol supplementation during pregnancy TOX/2024/45

60. Professor Peter Barlow declared a direct commercial interest as his employer intended to make an application for the authorisation of vitamin D supplements to the Medicines and Healthcare Products Regulatory Agency (MHRA). It was agreed he was able to contribute to the discussion of this item but could not participate in the conclusions.. Dr Stella Cochrane and Dr Natalie Thatcher declared personal non-specific interests as their employers also sold supplements as part of their product range, although they did not directly work on them. They were able to contribute to discussions but could not participate in conclusions.

61. No other interests were declared.

62. This item was part of the ongoing programme of work on nutrition and maternal health being conducted by SACN. The work focuses on maternal outcomes during pregnancy, childbirth, and up to 24 months after delivery, with the COT advising on the effects of chemical contaminants and excess nutrients in the diet.

63. Following publication of the COT statement on the potential effects of excess vitamin D intake during preconception, pregnancy and lactation, SACN requested that the COT also review Calcidiol as an Annex to this statement, since

this was a more potent form of the vitamin.

64. Calcidiol (25 Hydroxycholecalciferol) has two times the bioavailability of vitamin D3. However, it was not necessarily more potent than vitamin D3 as neither were the biologically active form (i.e., 1, 25-dihydroxyvitamin D). Members requested that this point was reflected in the paper.

65. Members queried the paper's discussion of calcidiol having a shorter half-life than vitamin D3 but leading to a more rapid and sustained increase in serum 25(OH)D levels in paragraph 11.

66. The Committee pointed out that the majority of the human studies discussed were conducted in post-menopausal and vitamin D deficient women, and therefore were not specific to pregnant and lactating women. It was noted that this was due to the limited data available in literature on calcidiol consumption during pregnancy.

67. Members noted that the single relevant study included in the paper looked at women aged 18-50 years who made up 65% of the study population. There was a single pregnancy, but it was in the placebo arm of the study.

68. Members agreed that calcidiol supplement use did not appear to be associated with risk to the fetus or mother and that pregnant women did not appear to be a sensitive sub-population since pregnant women were included in the Tolerable Upper Level of 100 µg/day established for adults. Therefore, extrapolating from the studies of post-menopausal and vitamin D deficient women might not be inappropriate. The Committee concluded that the limited data available for pregnant women was a major uncertainty in the assessment and requested that the relevance of the studies and their limitation be discussed in the conclusions.

69. The influence of genetic polymorphisms (particularly mutations in CYP 24A1) on the risk of hypercalcemia was raised, as these individuals would be more susceptible to developing hypercalcemia. The prevalence of this genotype was noted to be as high as 4-20%, however, Members were informed of a study assessing a Scottish population that reported the overall incidence of hypercalcemia to be 0.1-2%.

70. It was noted that the condition associated with polymorphisms in CYP 24A1 was recessive and was rare. It was often detected in childhood as idiopathic hypercalcemia and tended to be a chronic rather than an acute symptom.

Moreover, these individuals would be advised by their health care practitioner to avoid excess supplementation with vitamin D and its derivatives.

71. Other mutations such as those in the vitamin D receptor (VDR) were noted, and the Committee were informed that this was covered in the SACN report on vitamin D, but that SACN did not make recommendations based on genotype. Members queried if the TUL for vitamin D equivalents (VDE) of 100 µg/day was inclusive of individuals with this genetic polymorphism, and if a lower TUL should be set for such individuals. However, it was agreed that it would be impractical to do so. It was noted that the current HBGVs established by the Advisory Committee on Novel Foods (ACNFP) and by EFSA would have been set using data from mixed populations that would include some individuals with these genetic polymorphisms.

72. Overall, Members were content with the discussion on genetic polymorphisms and hypercalcemia risk in paragraph 103 of the paper and agreed that the COT could not provide any further input.

73. Members also discussed the possibility of having separate TULs for vitamin D3 and calcidiol, but it was considered that consumers may misinterpret the upper limits as being separate and combine their intakes of vitamin D3 and calcidiol, thus resulting in excessive intakes.

74. Members discussed the endogenous synthesis of vitamin D in the skin via UVB radiation, which may lead to variation in baseline levels due to factors such as ethnicity, changes in season and time outdoors. Whilst it was acknowledged that vitamin D synthesised in the skin does not contribute to toxicity due to the feedback mechanisms present, the Committee requested that more information on the influence of ethnicity (including differences in vitamin D requirements) and seasonality is added to the paper, possibly as a sub-section.

75. The Committee also asked that the conclusion was more inclusive of the effects of calcidiol exposure from both the diet and supplements, rather than concluding on them separately.

76. The Committee were unclear on the differences between the proposed HBGV by the ACNFP of 40 µg/day and the level EFSA established as safe (i.e. up to 10 µg/day). Members acknowledged that the ACNFP TUL derived from dividing the TUL of 100 µg/day by a conversion factor of 2.5, to account for the greater bioavailability of calcidiol. However, they found it unclear how the level EFSA established as safe (i.e. up to 10 µg/day) was derived. It was thought that this

was likely to be the level that the applicant had requested for authorisation rather than a maximum safe level *per se* but this should be clarified.

77. Members were unable to conclude on an appropriate HBGV value for risk characterisation for calcidiol and requested that the discussion paper is to return to the Committee with the suggested revisions discussed in the meeting.

Item 9: Developing COT guidance TOX/2024/45

78. The COT has agreed to update its guidance on toxicity testing and its supporting principles. To start this work, the COT held a workshop in May 2023. The workshop aimed to focus on identifying the principles that would underpin the development of the guidance. It was considered that the COT should identify existing frameworks and guidance and use or adapt these as necessary, and that it should encourage the integration of new approach methodologies (NAMs), using the best science available.

79. The purpose of paper TOX/2024/45 was to start the work developing the new COT guidance and seek the Committee's agreement on the way forward, including whether establishing a working group would be the most appropriate approach. The paper included links to existing guidance by EFSA and other organisations, and it contained a proposal on the structure of the COT guidance, based on the Committee's discussions to date. It was proposed that a main guidance document is produced which contains the overarching principles and then additional guidance documents provided on specific topics that link to the main document.

80. Members were asked whether they were content with the proposed format of the guidance and to consider how they would wish to proceed with this work, for example, if they agreed with establishing a working group to initially develop the main guidance document. They were also asked on what topics COT guidance should be developed and on what existing guidance could be used or signposted in the main COT guidance document. Members were also asked whether the COT should develop sector-specific guidance or whether this should be considered by the relevant JEGs once the main COT guidance document setting out the general principles was finalised.

81. It was suggested that the terms of reference of the COT should also be reviewed, both in terms of substance types (e.g. whether cosmetics are included) and science domains (e.g. whether antimicrobial resistance was in the COT's

remit).

82. Members agreed that the 3/6Rs (replacement, reduction and refinement of animal testing, but also recently extended to include the reproducibility, relevance and regulatory acceptance of alternatives), which include NAMs, should be taken into account. It is important that evaluations were based on the weight of evidence. A Member noted the need for the Committee to consider how NAMs could be used to fill the data gaps it often identified.

83. It was noted that EFSA has produced many guidance documents, of which some were very useful and relevant. It was suggested that each of the EFSA guidance documents should be considered to determine whether there are any areas that the COT disagreed with strongly, so that UK-specific guidance would be needed in those areas. It was also suggested that a hybrid approach may be possible, making use of existing guidance and adapting it to be UK centric.

84. It was considered important to bring the JEGs into the discussion. It was suggested that sector-specific guidance could be produced by the COT and the JEGs working together, perhaps in joint working groups.

85. It was noted that the COT and its sister Committees on carcinogenicity (COC) and mutagenicity (COM) represent only a small number of the Scientific Advisory Committees (SACs) that advise government. It was agreed that consideration should be given to including other SACs that advise Government Departments outside the FSA and DHSC. It was also suggested that the international perspective should be considered, and that the COT may need to influence the development of OECD guidance. However, it was also noted that a UK perspective was needed in some instances. It was stressed that the COT Secretariat was jointly led by the FSA and UKHSA and the COT has a wide remit.

86. It was suggested that the Committee should review the level of technical understanding expected of lay audiences when producing its lay summaries. It was agreed that this work should be taken forward either as part of the proposed working group or separately.

87. Members agreed that a working group should be established, initially to discuss the development of COT guidance in more detail, to consider the questions in the paper, consider what other factors should be taken into account and consider existing EFSA guidance. It should include representation from the JEGs and possibly other groups at a later stage. Volunteers were sought to participate in the working group.

Item 10: Update on the work of other FSA Scientific Advisory Committees - for information

88. This paper was circulated for information, but Members should contact the Secretariat if they have any questions.

Item 11: Any other business

89. There was no other business.

Date of next meeting

90. The next meeting of the Committee will be held on the 4th of February 2025 via Microsoft Teams.

Secretariat December 2024