Meeting

Draft Minutes of the 20th May 2025 COT Meeting

Minutes of the meeting of the Committee at 10:00am on the 20th May 2025 at Clive House and via Microsoft Teams.

Present

Chair:	Reverend Professor Lesley Stanley

COT Members:

Professor Gary Hutchison

Professor Thorhallur Ingi Halldórsson

Dr David Lovell

Professor Shirley Price (Deputy Chair)

Dr Cheryl Scudamore

Dr Simon Wilkinson

Professor Philippe Wilson (until item 8)

Dr Steven Enoch

Professor Peter Barlow

Dr Chris Morris

Dr Meera Cush

Mr Gordon Burton

Dr Andreas Kolb

Dr Alison Yeates (absent for Item 9)

Mr Nick Richardson

Dr Bryony Ross

Dr Michelle Bellingham

Professor Martin Clift

Dr Aravindan Veiraiah

Professor Mohammad Qasim Chaudhry (until Item 7)

Dr Tarek Abdelghany

Ms Christel Wake

Dr Antonio Peña Fernández

SACN Liaison:	Professor Paul Haggarty (Items 7 and 8)
Science Council:	Mr Tom Oliver (Chair’s introduction)

Ms Cath Mulholland - FSA Scientific Secretary

Dr Tahmina Khan

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 Frederique Uy

Secretariat: Food Standards Agency (FSA)

Ms Jocelyn Frimpong-Manso

Ms Sophy Orphanos

Dr Gaetana Spedalieri

Mr Thomas Hornsby

Dr Emily Hudson

Dr Aaron Bradshaw

Dr Katie Schulz

Ms Katie Wetherall

Ms Rachel Kerr

Mr James Metcalfe

Ms Yoana Petrova

Ms Polly Bevan

Mr Andy Axon

Ms Abigail Smith

Secretariat: UKHSA - UK Health Security Agency	Ms Britta Gadeberg Ms Sanyukta Pallavi Mr Steve Robjohns
Assessors: UKHSA - UK Health Security Agency	Dr Ovnair Sepai
Assessors: DBT- Department of Business and Trade	Ms Frances Hill
Invited Experts: RSM UK Consulting LLP – Presenting/Observing TOX-2025-20 Safety of nitrates and nitrites (Reserved)	Ms Shraddha Kaur (presenter) Mr Will Harris (presenter) Ms Sofia Reva (presenter)
FSA Officials:	Mr Adam Hardgrave (Items 5 and 6) Ms Helen Twyble Dr Joseph Shavila Mr Allan Shivembe Ms Pamela Iheozor-Ejiofor Ms Rhoda Aminu
Officials from other Government Departments:	Ms Krystle Boss - FSS – Food Standards Scotland:

Observers:	Ms Donna Webley Ms Emma Sutton Mr Steve Hodgson (item 6). Dr Stephen Ruckman (Principal Consultant; from item 7).

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Announcements

1. The Chair welcomed Members and other attendees to the meeting.

2. This was the last meeting for Dr Silvia Gratz, whose term of ap pointment expires at the end of May 2025. This was also the last meeting for Scientific Advisory Committee on Nutrition (SACN) liaison Member Professor Paul Haggarty as he will be stepping down from SACN this month. Members would be updated on SACN liaison in due course.

3. The Chair and Secretariat thanked Dr Gratz and Professor Haggarty for their valuable input into the work of the Committee.

4. The Reverend Professor Lesley Stanley was welcomed to her first meeting as the new Chair of COT. In addition, Professor Martin Clift, Dr Bryony Ross, Dr Michelle Bellingham, Professor Qasim Choudhry, Ms Christel Wake, Dr Arvind Veiraiah and new Associate Members Dr Tarek Abdelghany and Dr Antonio Pena Fernandez were welcomed to their first meeting of the Committee.

5. A number of external observers were present. Ms Shraddha Kaur, Mr Will Harris and Ms Sofia Reva from RSM UK Consulting presented Item 6 on nitrates. Ms Donna Webley, Ms Emma Sutton and Mr Steve Hodgson from RSM UK Consulting observed Item 6.

6. External observers Dr Stephen Ruckman, of TSG consulting and Dr He len Crawley of the Lizzie Vann Foundation were also present for the unreserved items.

Interests

7. 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

8. Apologies were received from COT Members Professor Mireille Toledano and Dr Silvia Gratz. Apologies were also received from Ms Jackie Healing (Science Council Liaison Member), Dr Minako Takamiya Allen and Helen McGarry (HSE Representatives), Emma Bradley (FERA), and Dr Sam Fletcher (Veterinary Medicines Directorate).

Item 2: Introduction from the new Chair

9. The new COT Chair, Reverend Professor Lesley Stanley, introduced herself to the Committee setting out her thoughts on how she hoped to approach the role. The new and existing Members and Associate Members then briefly introduced themselves.

Item 3: Minutes of the of the Tuesday 25th March 2025 meeting (TOX/MIN/2025/02)

10. It was noted that the Chair and Deputy Chair had reviewed the minutes of the March meeting and were happy that they reflected the Committee’s discussions. Several comments on the draft minutes had been submitted to the Secretariat in advance of the current meeting and incorporated.

11. No further amendments were made to the draft minutes or reserved minutes. They were agreed to be an accurate record.

Item 4: Matters arising

Joint Expert Group (JEG) updates

Additives, Enzymes and other Regulated Products Joint Expert Group (AEJEG)

12. The last standard AEJEG meeting took place on the 1st of April. The following items were presented:

i. Matters Arising – Flavourings guidance: weight-of-evidence document for exposure assessment.

ii. Draft Committee Advice Paper (CAD) RP41 – Extension of use of curcumin (E 100) to a new food category, “egg analogues”. It was agreed that the section on exposure assessment would be brought forward to the next AEJEG meeting under Matters Arising, while the remainder of the document would be signed off via correspondence.

iii. RP733 Application – An update paper, discussion paper, and cover paper were presented regarding the application for authorisation of soy leghemoglobin derived from *Pichia pastoris* as a flavouring precursor for plant-based meat alternatives in the United Kingdom. A further request for information (RFI) will be sent to the applicant.

13. The AEJEG Smoke Flavourings Working Group (SFWG) met on the 26th of March 2025 to review the final two summary documents: RP1614 and RP1615. The next standard AEJEG meeting is scheduled for the 4th of June 2025. A joint COT/COM meeting will take place on 19th of June 2025 to peer review the CADs for smoke flavourings.

14. The COT Members were updated on the next phase of the smoke flavouring applications, now that the assessment of the genotoxic potential of the eight applications has been concluded.

15. Members of the COT who are also part of the AEJEG SFWG commented that this workstream has been intensive and praised the efforts of the Secretariat.

Food Contact Materials Joint Expert Group (FCMJEG)

16. COT Members were informed that the updated statement on environmentally sourced plastics, including Ocean-Bound Plastics, was published

in May 2025 and was available to view on the FCMJEG area of the COT website and as a news story on the FSA website.

17. The assessment of the application for calcium tert-butylphosphonate is progressing and will be published in due course.

18. Currently, one application is at the Request for Information (RFI) stage (RP2263 - agar palmitate). Two recycling process applications are under assessment (RP1415 and RP1898).

19. The FCMJEG did not meet in April 2025. At the next meeting, planned for 28th May 2025, the Group will review two novel recycled plastic applications as part of the ongoing competent authority audit Further information on a recycling process and a plastic additive application will also be considered (RP1415 and RP2147, respectively).

Flavourings guidance: weight-of-evidence document for exposure assessment (Reserved) TOX/2025/18

20. No interests were declared.

21. This item is currently being treated as reserved.

Subgroups and working groups

COT Guidance

22. COT Members were reminded of ongoing work to update the COT Guidance. Members who wished to contribute to the working group were asked to contact the Secretariat.

Joint SACN/COT Working Group (WG) on plant-based drinks

23. The last meeting of the joint COT/SACN plant-based drinks working group would be held at the end of May 2025 with the aim of finalising the draft report. This had been significantly restructured, though without substantial changes to the text. The final WG report is required to be approved for publication by COT and SACN. Members agreed to review and approve the report via correspondence in order to expedite publication.

AI Risk Assessment Workshop

24. The next COT workshop was scheduled to take place on the 22nd of October 2025. The Committee were informed that the theme would be the use of artificial intelligence (AI) in risk assessment. COT Members were asked to consider any specific topics or particular speakers that could be included in the agenda and to send any ideas to the Secretariat.

25. Members made some initial comments following the update. These included consideration of the importance of interpretability, data ethics and data ownership. The Secretariat informed the Committee that a scoping paper on AI in risk assessment considering these points would be presented prior to the workshop.

Publications

26. The Committee were informed that the report of the 2024 COT workshop “Gut reactions: Xenobiotics and the microbiome” will be published in the coming weeks.

Item 5: Committee Advice on the Authorisation of the substance Blue Microalgae Extract (Blue Galdieria Extract) for Use as a New Food Additive in the ‘Colour’ Functional Class. (RP507) (Reserved) (TOX/2025/19)

27. A declaration of interest was made by Dr David Lovell. He had provided the Additives, Enzymes and other Regulated Products Joint Expert Group (AEJEG) with statistical advice on the 90-day subchronic toxicity study. The Committee agreed that this did not preclude him taking part in the discussion. No other interests were declared.

28. Phycocyanin-rich extracts are obtained from blue microalgae extract to provide a blue colouring but were not currently authorised for use. At the time of this meeting, no pure phycocyanins from any source were authorised as food additives in the EU, although phycocyanin-rich extracts from *Spirulina* were used as food colourants.

29. The AEJEG first considered an application for the safety of the authorisation of blue microalgae extract (Blue *Galdieria* extract) for use as a new food additive in the ‘colour’ functional class in February 2022.

30. The AEJEG concluded that sufficient information had been provided to allow the use of blue microalgae extract as a new food additive under assimilated Regulation (EC) No 1333/2008.

31. The COT was asked to consider the CAD drafted by the AEJEG on the use of blue microalgae extract.

32. This item is currently being treated as reserved because it contains commercially confidential and sensitive data.

Item 6: Safety of Nitrates and Nitrites as Food Additives- Presentation from RSM UK Consulting LLP (Reserved) (TOX/2025/20)

33. Professor Thorhallur Ingi Halldórsson declared an interest. He had chaired a working group for the Danish Environmental Protection Agency regarding revising the parametric value of nitrate in drinking water. This did not preclude him from taking part in the discussion. No other interests were declared.

34. This item is currently being treated as reserved because it is not yet, published.

35. The RSM UK Consulting team delivered a presentation on their FSA-funded literature review of the safety of nitrates and nitrites as food additives.

36. Members discussed the content of the presentation and report and provided minor comments. Members requested that future documents provide more information on the chemistry involved, especially in cases where substances can undergo chemical and/or metabolic interconversions.

Item 7: Discussion paper on the effects of calcidiol supplementation during preconception, pregnancy and lactation (TOX/2025/21)

37. Professor Peter Barlow declared a direct commercial interest. He is a named inventor on a patent covering a composition which may include Vitamin D for therapeutic use, which could be subject to future commercialisation by his employer through the Medicines and Healthcare products Regulatory Agency (MHRA). This was considered a specific, personal interest and it was agreed that

he should not contribute to the discussion of this item.

38. Dr Meera Cush and Rev Prof Lesley A. Stanley declared interests as they have both been involved in preparing CADs published by the Advisory Committee on Novel Foods and Processes (ACNFP) panel. However, it was agreed that they were able to contribute to discussions.

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

40. Calcidiol was last considered by COT in December 2024. Members had requested the item return to the COT to clarify a perceived discrepancy between the levels established as safe by EFSA and by ACNFP, the latter relating to a novel food application for calcidiol.

41. The discrepancy between levels reported as safe for the novel food application for calcidiol was a misinterpretation of the ACNFP Safety Assessment “Calcidiol (25-hydroxycholecalciferol monohydrate) as a novel food for use in food supplements” that was published in 2024. The Committee was informed that the ACNFP agreed with the applicant’s proposed intake of 10 µg/day for adults, which was also agreed by EFSA. However, the ACNFP established an additional tolerable upper intake level (TUL) of 40 µg/day to identify a level that would be safe if consumers were to go beyond the proposed intake of 10 µg/day. This was considered a possibility by the ACNFP as the product is available over the counter and would be used unsupervised by consumers. This clarified that there was no difference between the EFSA and ACNFP advice on Tolerable Upper Levels.

42. The Chair provided Members with some brief background on calcidiol, and the purpose of its review by the ACNFP. Calcidiol is not intrinsically more potent than vitamin D3 but is more bioavailable so the same dose can result in higher circulatory levels of 25-hydroxyvitamin D than would arise from the equivalent vitamin D dose. Calcidiol has a shorter half-life and is more hydrophilic than vitamin D.

43. The ACNFP position statement largely followed EFSA’s approach. However, it was noted by ACNFP that the novel foods applicant was unable to confirm whether consumption of calcidiol could have the potential to disrupt vitamin D homeostasis. However, as there was no evidence to demonstrating disruption to homeostatic mechanisms, the ACNFP did not consider calcidiol to be

of toxicological concern.

44. Calcidiol has been used in animal feed but there was still uncertainty around its bioavailability in animal models.

45. Members were informed that the ACNFP's position statement and the EFSA opinion on calcidiol were included as evidence in the COT review due to the limited data set for calcidiol in the published literature.

46. It was noted that the 90-day study (Thiel et al. (2007)) cited in paragraph 23 was unpublished and should be caveated accordingly. In addition, it was noted that the Guerra López et al. (Nutrients, 16(2), p.306, 2024) study cited in paragraph 48 reported only a single clinical observation.

47. If the discussion paper were to return to the COT, Members requested that all toxicological data relating to the target population was discussed first and that it was highlighted that the target population being assessed (i.e. pregnant and lactating women and women attempting conception) was underrepresented in the available evidence package. In addition, the Committee noted that the toxicological dataset for calcidiol was limited and not relevant to the target population. It was, therefore, suggested that paragraphs 33-40 be re-positioned in the discussion paper because they contained data on population groups outside the target population.

48. Members requested that consistent units be used to describe doses throughout the discussion paper. The duration of the human studies cited in the discussion paper should be reported in all cases.

49. Members sought clarification on the conversion factor of 2.5 used by EFSA and by ACNFP to establish the TUL. The conversion factor can vary with dose. For example, at doses of vitamin D derivative > 25 µg the conversion factor became 1.3 and therefore using 2.5 would make the TUL of 40 µg/day extremely conservative. However, it was noted that the 2.5 conversion factor was an average of the conversion factors that could be used and was used because it was the one that had been used in human studies.

50. Regarding the exposure assessment, Members agreed that estimated intakes were not reaching the levels of the Health Based Guidance Values (HBGV) and therefore were not of concern. Members suggested it may be useful to revise exposure calculations with the assumption that the target population is following the NHS dietary advice issued to pregnant women.

51. The two vitamin D derivatives in the exposure assessment were queried by Members and were confirmed be to different forms of calcidiol i.e. 25-hydroxyergocalciferol and 25-hydroxycholecalciferol. Members were informed that other forms of vitamin D (D2 and D3) were not accounted for in the exposure assessment. It was suggested that the exposure assessment be expanded to include other forms of vitamin D to estimate aggregate exposure to vitamin D derivatives.

52. Members questioned whether excess vitamin D or calcidiol consumption might cause neurological effects. The main adverse effect noted was hypercalcemia; there was no suggestion of potential neurological effects.

53. The Committee asked the Secretariat to check the statement that 'No intoxication as measured by hypercalcemia has been reported in humans at serum 25- hydroxycholecalciferol levels below 500 nmol/L' in paragraph 27, as different values have been reported elsewhere in literature.

54. The COT confirmed they were not in disagreement with EFSA's conclusion on the level established as safe and agreed that at present, there was no evidence that there was excess exposure to vitamin D in the population.

55. Members were reminded of SACN's requirements, which include information on the consequences of possible exceedances of calcidiol supplementation and identification of a clear safe upper limit where this existed. SACN also required confirmation on the proportion of women of childbearing age that may be exceeding the safe upper limit, in order to aid any future decisions on fortifying food.

56. Further discussions would be held amongst the Chair, Secretariat and Rapporteurs for this item to decide how to present the committee's conclusions on calcidiol and Vitamin D.

Item 8: First draft statement on mercury in the maternal diet (TOX/2025/22)

57. No interests were declared.

58. In 2020 the COT discussed a prioritisation paper on substances that could be considered for risk assessment by the COT as part of the programme of work assessing risks from the maternal diet. This feeds into the 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 (mercury, lead, cadmium and arsenic) should be considered in separate papers. This statement focuses on the risks posed to maternal health by mercury in the diet and the environment.

59. In February 2025 the Committee considered a discussion paper (TOX/2025/03) which reviewed the available data on toxicity of inorganic mercury and methylmercury (MeHg) to maternal health. It included a risk assessment of total dietary exposure to mercury in women of childbearing age in the United Kingdom (UK). Overall, the Committee concluded that the paper was clear in its description of mercury toxicology. Recently published data confirmed current knowledge on the toxicity of inorganic mercury and MeHg and did not constitute a basis for revising the current HBGVs set by EFSA. The Committee concluded that total exposure to mercury from the diet was below the EFSA HBGVs. Based on the current UK exposure data there were, therefore, no concerns to women of maternal age. The HBGVs offer adequate protection for this sub-population.

60. In accordance with Members' comments on the discussion paper a draft statement had been prepared. This included a section on exposure to mercury via contamination of dietary supplements and reiterated the UK Government's advice on foods to avoid during pregnancy. The toxicity and recently published literature sections had also been condensed as the Committee concluded that the new data confirmed current knowledge and did not constitute a basis for revising the current HBGVs.

61. Regarding paragraph 25, Members queried how mercury concentrations in cord blood could be up to twice maternal blood concentrations and asked that this paragraph be expanded and clarified.

62. The item rapporteurs noted that paragraph 50 states that a mean of the MeHg concentration in hair from the Faroes Islands and the Seychelles study populations that reflects exposures that would have no appreciable effect on the offspring was used to derive a HBGV for MeHg. However, the Members suggested that using the slightly lower Seychelles maternal hair mercury concentration alone rather than a mean of two populations would provide a more conservative HBGV, given that mercury shows cumulative toxicity.

63. The Committee questioned whether the latest report on the risks and benefits of fish consumption published by FAO/WHO in 2024 should be mentioned in the statement, since the main source of mercury exposure is seafood. It was

noted that SACN would consider the benefit of fish consumption, whereas COT would address risks. Therefore, the FAO/WHO report could be cited in the statement for completeness, but only in terms of assessing the risk of seafood consumption.

64. The Committee requested that the structure of the document should separate the discussions on inorganic and organic mercury throughout the whole statement rather than just the toxicology and ADME sections to improve the readability of the document.

65. Members asked the Secretariat to clarify throughout the statement what effects are observed in the mother, and which are observed in the offspring when referring to adults.

66. The Committee requested the Secretariat to double-check the limits of detection and quantification for the concentration of mercury in water in Scotland and NI provided in paragraphs 63 and 64, since they seem to have been interchanged.

67. It was noted by a Member that the National Diet and Nutrition Survey (NDNS) tended to underestimate energy intake by around 30%. If the underestimation is accounted for and the intake from dietary supplements was also considered, the total dietary weekly intake of mercury might exceed the tolerable weekly intake for MeHg of 1.3 µg/kg bw in the highest exposure scenarios and would need to be addressed in the conclusions.

68. The Committee suggested that the guidance provided in the conclusions should be tailored to the different stages highlighted in the introduction (i.e. pre-conception, pregnancy, breast-feeding and up to 24 months after delivery).

69. Lastly, the Committee noted that the statement refers to opinions of other authorities throughout. It should be made clear when the committee is endorsing other authoritative opinions, on what primary evidence those opinions are based and what primary evidence the committee has itself considered.

70. The Secretariat would address all comments and prepare a second draft statement for review by the Committee at a later meeting.

Item 9: Statement on the derivation of a health-based guidance value for antimony – First Draft

(TOX/2025/23)

71. No interests were declared.

72. 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 HBGV for antimony (Sb). This topic was initially considered at the COT meeting in October 2024 (TOX/2024/38). To evaluate the most appropriate study and endpoint to select for the critical effect, during its meeting in February 2025 the Committee reviewed information on additional studies from which the authors reported lower points of departure (TOX/2025/04).

73. During the February meeting, the COT identified a No Observed Adverse Effect Level (NOAEL) of 6,000 µg Sb/kg bw/day from the Poon et al. study (Food and Chemical Toxicology (1998), 36(1), pp.21-35) based on decreased body weight gain and reduced food and water consumption in adult rats. This was chosen as the appropriate point of departure (POD) to use in deriving a HBGV for antimony. The Committee recommended an uncertainty factor (UF) of 300, 10 for interspecies variation, 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.

74. During the May meeting Members considered the first draft statement which is intended for risk managers and policy makers and will be published on the COT website. Minor changes, including ensuring consistency of units and providing further details regarding the NTP study (NTP Tox 11. NIH Publication No. 92-3130 1992), were suggested. In addition, it was agreed a Lay Summary would be prepared to accompany the statement.

75. The Committee concluded that the table in Annex A was useful to support the statement and should be included in the final statement.

76. Appropriate UFs for extrapolating from a subchronic toxicity study to a TDI for chronic exposure were discussed. At the February meeting the COT had agreed an uncertainty factor of 3 to extrapolate from the subchronic study to a chronic exposure. It was noted that the current EFSA guidance recommends factor of 2 for this extrapolation, but the Committee agreed that the factor of 3 should be used as this allows for additional uncertainty in the extrapolation.

77. It was agreed that further editorial amendments should be sent to the Secretariat, and the statement and lay summary would be cleared by Chair's action.

Item 10: Update on the work of other FSA Scientific Advisory Committees – For information (TOX/2025/24)

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

Item 11: Any other business

79. There was no other business

Date of next meeting

80. The next meeting of the Committee will be at 10:00 on Tuesday 15th July 2025 via Microsoft Teams.

Secretariat

May 2025