Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Meeting of the Committee at 10:00 on 15th September via Skype and TEAMs

Present		
Chair:	Prof Alan Boobis	
COT Members:	Dr Phil Botham	
	Dr Caroline Harris	
	Dr René Crevel	
	Dr David Lovell	
	Dr Mac Provan	
	Prof Faith Williams	
	Dr Michael Routledge	
	Dr Cheryl Scudamore	
	Dr Natalie Thatcher	
	Prof Matthew Wright	
	Prof Gunter Kuhnle	
	Dr Sarah Judge	
	Dr Stella Cochrane	
	Ms Jane Case	
	Ms Juliet Rix	
	Prof Ken Ong	
	Prof Paul Haggerty	
Food Standards Agency (FSA) Secretariat:	Ms Cath Mulholland	FSA Scientific Secretary
	Dr David Gott	
	Dr Douglas Hedley	
	Mr Barry Maycock	
	Dr Alexander Cooper	
	Dr Barbara Doerr	
	Ms Cleanncy Hoppie	
	Dr Olivia Osborne	
	Dr Joe Shavila	
	Ms Chloe Thomas	
	Ms Sabrina Thomas	
	Ms Chara Tsoulli	
	Ms Frederique Uy	
	Ms Aisling Jao	
	Ms Jocelyn Frimpong-Manso	
Public Health England (PHE) Secretariat:	Ms Britta Gadeberg	PHE Scientific Secretary
Invited Experts and Contractors:	Dr Ruth Bevan	IEH
	Mr Joe Brennan	nabim (Item 3)
	Mr Alex Costigliola	nabim (Item 3)
	Ms Alison Gowers	PHE Committee on the Medical Effects of Air Pollutants (COMEAP) Secretariat (Item 4)

	Dr Mark Miller	COMEAP (Item 4)
	Ms Christina Mitsouka	PHE COMEAP Secretariat (Item 4
Assessors	Ms Louise Dearsley	Health and Safety Executive (HSE)
	Prof Tim Gant	PHE
	Ms Gillian McEneff	Department for Business, Energy and Industrial Strategy (BEIS)
	Ms Elizabeth Lawton	Department for Environment Food and Rural Affairs (DEFRA)
	Dr Daphne Duval	PHE
	Mr Ian Martin	Environment Agency (EA)
	Dr Sam Fletcher	Veterinary Medicines Directorate (VMD)
FSA and other Officials:	Prof Robin May	FSA
	Mr Ross Yarham	FSA (Item 3)
	Dr Alan Dowding	FSA (Item 4)
	Dr David Mortimer	FSA
	Mr Mark Willis	FSA
	Ms Azuka Aghadiuno	FSA
	Ms Beth Rendle	FSA
	Ms Bethan Davies	FSA
	Mr Richard Annett	FSA NI
	Mr Kerry Gribbin	FSA NI
	Ms Sharon Gilmore	FSA NI
	Ms Krystle Boss	FSS
	Ms Laura Wilson	FSS
	Dr Tim Marczylo	PHE
	Ms Rachel Elsom	PHE
	Mr Liam Johnstone	BEIS

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Announcements

1. The Chair welcomed Members and other attendees.

2. Professor Robin May, the new FSA Chief Scientific Advisor attended the early part of the meeting to introduce himself to the Committee and explain his role. He looked forward to working with the Committee.

3. The Chair introduced Jocelyn Frimpong-Manso, a new Member of the Secretariat.

4. Members were informed that the new COT website was now live, and the Chair thanked the Secretariat for all their hard work setting it up. Members were asked to notify the Secretariat if they identified any problems.

Interests

5. 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

6. Apologies have been received from COT Members Professors Gary Hutchison, Maged Younes, John Foster, Mireille Toledano and Dr James Coulson, Professor John O'Brien from the Science Council, and Ms Claire Potter from the COT Secretariat. Ms Louise Dearsley attended in place of Ms Valerie Swaine, the HSE Assessor.

Item 2: Minutes from the meeting held on 7th of July 2020 (TOX/MIN/2020/05)

7. The minutes of the July meeting were agreed subject to minor amendments to Items 5 and 8 as below:

8. For Item 5, Members noted some repetition of information in paragraphs 29 and 32 and asked for the addition of text in paragraph 25 to clarify that these were "mitigation measures". To avoid misinterpretation in paragraph 33, Members asked "percentage of allergic population" to be changed to "relevant population", as it could otherwise be misunderstood as total population.

9. Members noted for Item 8 that "aggregate exposure" would be the exposure to the same substance by different routes and therefore suggested "cumulative exposure" or "combined exposure" as a more appropriate and accurate wording.

Item 3: Matters arising from previous meetings

COT meeting, 10th March 2020

10. The COT statement and lay summary on the human microbiome paper had now been published.

11. The COT statement and lay summary on Electronic Nicotine (and Non-nicotine) Delivery Systems (E(N)NDs) had now been published. There had been some positive media interest in the topic in which the Chair had been involved.

COT meeting, 5th May 2020

12. The COT position paper on the risk of cannabidiol (CBD) in CBD products had been published. It had been well received as providing a useful summary of the available information and discussions to date. The Chair informed Members that he had attended a meeting of the Advisory Committee on Novel Foods and Processes (ACNP) where CBD had been discussed, this included ACNFP discussion of the COT position paper as well as consideration of the data that might be needed to support authorisation of CBD products.

COT meeting, 7th July 2020

Paragraph 9

13. Due to the continuing COVID situation, the venue for the proposed workshop on PBPK modelling in December 2020 has been cancelled. The Secretariat was considering how best the workshop could be delivered. Members were therefore asked to continue to hold the date.

Paragraph 18

Allergen risk assessment for adventitious contamination by soya in wheat flour milled and consumed in the UK. TOX/2020/39

14. No interests were declared.

15. Mr Joe Brennan and Mr Alex Costigliola from the National Association of British and Irish Millers (nabim) were in attendance for this item.

16. At the COT meeting on the 7th July 2020, a risk assessment (TOX/2020/31) of the adventitious contamination by soya in wheat flour milled and consumed in the UK was presented, including current industry monitoring data and discussion of reference dose values for soya protein allergy.

17. Following the Committee's discussion, the risk assessment was updated to address the comments made and to include the key conclusions and the messages to risk managers as was agreed at the July meeting. The updates were as follows:

a. The use of a set allergen action level to inform decisions on risk communication of soya contamination in wheat flour by food businesses selling raw/bulk product intended for further processing was not appropriate due to variation in the level of inclusion in final products, consumption

amounts, and the potential effects of processing on the allergenicity and detectability of soya.

b. This current application of a set action level at the raw ingredient supply level may hinder effective communication of health risk through the supply chain and the ultimate decision on the necessity to communicate risk to the final consumer via a precautionary allergen statement e.g. 'may contain'.

c. Alternative risk management approaches would need to be explored, including business to business communication of robust quantitative cross contact information throughout the supply chain to the final product producer. Other sources of soya contamination in the supply chain should be assessed and communicated at each stage in the supply chain.

18. Members confirmed that the points for revision had been completed satisfactorily and approved this version of the risk assessment as final, subject to an addition/clarification to the conclusions to note that, in the absence of a set action limit applied at the raw/bulk ingredient level, FSA risk managers would need to consider how the risk to soya allergic consumers would be mitigated by communicating industry risk assessments and analytical data to the end product manufacturer, and what actions would be required of them.

19. Where the risk assessment referred to the allergic population, it was agreed that the text should specifically state that this related to the population allergic to soya since the other regulated allergens have their own reference doses.

20. It was noted that there was no systematic way of reporting allergic reactions to food in the UK. Allergy can range dramatically in severity and milder reactions, including those that may be expected in the context of this risk assessment, were generally less likely to be reported, as they would be self-resolving or self-medicated, compared to more severe reactions that might require emergency and medical attention. However, the FSA recognised the importance of more systematic reporting in general and it was highlighted that the FSA was in the process of establishing the feasibility of a mechanism for reporting of reactions involving food allergens. A project was also underway to develop a prospective anaphylaxis register to better understand circumstances of anaphylactic reactions to food.

Item 4: Second draft overarching statement on Microplastics. TOX/2020/40

21. No interests were declared.

22. Dr Mark Miller from the Committee of the Medical Effects of Air Pollutants (COMEAP) and Ms Alison Gowers, and Dr Cristina Mitsakou from the COMEAP Secretariat (PHE) were present as invited experts for this item. Prof Boobis noted that he is also a member of COMEAP. Dr Ian Martin from the Environment Agency (EA), and Dr Alan Dowding from the Policy branch of the FSA were also in attendance.

23. The potential risks from exposure to microplastics have previously been discussed at COT meetings from October 2019 – March 2020. The draft overarching

statement, presented in Annex A, brought together these discussions, setting out the current state of knowledge, data gaps, and research needs with regard to this topic and summarising the conclusions reached to date. Following the finalisation of the draft overarching statement, it was intended that additional sub-statements would be drafted to address particular exposure routes or materials.

24. The COMEAP had published a statement on the evidence for differential health effects of particulate matter according to source or components in 2015. In this, the toxic mechanism of metals (present in non-exhaust sources of particulate matter such as brakes and tyres) associated with adverse health effects was related to their high oxidative potential. COT Members were provided a pre-publication copy of the COMEAP's upcoming statement on non-exhaust emissions for background information[1].

25. A short update on recent literature was also provided in TOX/2020/40.

26. Members noted the additional information presented in the cover paper, including the study by Halden et al., (in press); however, it was agreed that until the article had been published in full, no further comments could be made. Members expressed some reservations over the reliability of the cited *in vitro* data, where there was *in vitro* to *in vivo* extrapolation, for example, the Caco-2 models (e.g. Liu et al., 2020)[2] lacked the presence of a mucous barrier and were not necessarily comparable to the situation *in vivo*.

27. It was agreed that the European Food Safety Authority (EFSA) activity producing new guidance on the risk assessment of small particles should be noted in the next draft of the overarching statement.

28. The Committee requested that the Secretariat made clear the scope and purpose of the overarching statement so that it related directly to which Government department and/or committee body would have the responsibility to advise on the impact to public health from microplastics.

29. Members agreed that there was too much emphasis on tyre and road wear particles and that there should be a better balance between those and the other types of plastic particles covered by the overarching statement.

30. The Committee agreed with the approach of having an overarching assessment to be followed by subsequent sub-statements addressing particular exposure routes and/or materials where the in-depth toxicological information would be provided. However, the over-arching statement should clearly state that the detailed toxicology would be addressed in the sub-statements.

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[1] This is now published at: https://www.gov.uk/government/publications/non-exhaust-particulate-matter-from-road-transport-health-effects

[2] Liu, S., Wu, X., Gu, W., Yu, J. and Wu, B. (2020) Influence of the digestive process on intestinal toxicity of polystyrene microplastics as determined by in vitro Caco-2 models. Chemosphere 256, 127204

31. It was agreed that COMEAP and the COT should work together when reviewing the potential risks of microplastics via the inhalation route.

Item 5: First draft statements on the consumption of plant-based drinks in children aged 6 months to 5 years of age. TOX/2020/41

32. No interests were declared.

33. The Department of Health and Social Care (DHSC), PHE and the FSA were receiving an increasing number of enquiries regarding the use of plant-based drinks in the diets of infants and young children. The COT was therefore asked to consider the potential health effects of soya, oat, and almond drinks in the diets of children aged 6 months to 5 years of age.

34. Currently, the UK Government advises that parents should use only infant formula as an alternative to breast milk in the first 12 months of a baby's life. It further advises that whole cows' milk and unsweetened calcium-fortified milk alternatives, such as soya, almond and oat drinks can be given to children from the age of 1 year as a part of a healthy, balanced diet. Thus, it was assumed that exposure to these drinks from the age of 6 -12 months was only where the drink was used in cooking, but exposure was assessed as a main milk drink alternative from the ages of 1-5 years old.

35. Soya, almond and oat drinks were previously considered by the COT, most recently in paper TOX/2020/33. Paper TOX/2020/41 presented the first draft statements on soya, oat and almond drinks where the key safety concerns and the conclusions of the COT discussions were summarised.

Annex A- First Draft Statement on the potential risks from soya drink consumption in children aged 6 months to 5 years of age.

36. Soya drinks are a popular alternative to dairy products and their use has become increasingly widespread.

37. Soya products contain phytoestrogens (also known as isoflavones) which have been shown to produce some reproduction and developmental changes in animal studies, although the evidence for effects in humans from epidemiological studies is inconclusive.

38. Papers were presented to the COT in December 2019 and July 2020, reviewing the information available on the safety of these drinks. As children following plant-based diets were considered to be high consumers, the initial exposure assessment presented in December 2019 was refined by using several specialist sources of information that offered more realistic estimates of consumption in such children, to provide improved estimates of exposure to isoflavones.

39. In addition to exposure to isoflavones from soya drink itself, the contribution of other soya-based products, such as other alternatives to dairy products or to meat, to the diet was also considered.

40. The draft statement summarised the key safety concerns as well as conclusions from the discussions of the Committee.

41. It was agreed that further clarification was needed in the text regarding the conclusions of the 2013 COT review of phytoestrogens to ensure that the uncertainties were fully reflected. It was further agreed that in the conclusions section, the phrase “no potential concern” should be replaced with “less potential concern” to accurately reflect the views of the Committee.

42. The Committee agreed that information on the allergenicity of soya and the implications for consumer safety in these age groups, should be included.

43. A number of other minor editorial changes were also suggested.

44. It was agreed that the statement could be cleared by Chair’s action.

Annex B- First Draft Statement on the potential risks from oat drink consumption in children aged 6 months to 5 years of age.

45. No interests were declared.

46. In July 2020, a discussion paper on oat drinks was presented to the COT, where estimated concentrations of the mycotoxins HT-2 and T-2, deoxynivalenol (DON), and ochratoxin A (OTA) in oat drinks were assessed as these were considered to be the most likely hazards arising from the consumption of oat drinks. As these mycotoxins occur in other grains and foodstuffs, background exposures were also considered.

47. Exposure assessments were conducted using soya drink consumption data, as being the most representative for children following dairy-free or plant-based diets. Information on consumption by young children who may be consuming a mixture of different plant-based drinks was currently unavailable, therefore, the current approach assumed that consumption was exclusively of a single plant-based drink, therefore the consumption estimates for soya drinks were used in the assessment. This approach was agreed by the Committee as being the most appropriate approach, as some young children may develop a preference for one drink.

48. Members had concluded that there were no health concerns in respect of HT-2/T2 or 15-Ac-DON, 3-Ac-DON, DON, or the sum of 15-Ac-DON, 3-Ac-DON and DON, exposure. In respect of OTA, the Committee were unable to conclude whether the exposure estimates indicated a potential health concern since there were many uncertainties in the cancer endpoint used for risk characterisation, and it was unclear whether OTA was a genotoxic carcinogen and thus which MOE threshold value would be applicable.

49. Members made a number of minor comments on the structure and content of the draft statement.

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

Annex C- First Draft Statement on the potential risks from almond drink consumption in children aged 6 months to 5 years of age.

51. No interests were declared.

52. Almond drinks have lower nutritional value compared to soya or oat drinks; however, they are an alternative in cases where children refuse soya and oat drinks.

53. The mycotoxin, aflatoxin B1 (AFB1) was identified as an occasional chemical contaminant in almond nuts, which could potentially be transferred to almond drinks. Aflatoxin B1 was considered genotoxic and carcinogenic so its maximum levels set by the EU were based on the as low as reasonably achievable (ALARA) principle. The lack of analytical information on the effect of processing on aflatoxin levels in almonds during almond drink manufacture, as well as the lack of information on the actual AFB1 levels found in almond drinks, resulted in highly uncertain, overestimates, of exposure.

54. Estimates of exposure based on the Maximum Residue Levels set by the European Commission resulted in MOEs that were insufficient to provide adequate assurance of the risk to consumers. Overall, it was concluded that, in the absence of reliable occurrence data below current limits of detection, estimates of exposure would lead to an overestimation of risk and therefore were inadequate. The risk to health from exposure to AFB1 could not be determined.

55. Almonds contain cyanogenic glycosides, with levels being very high in bitter almond varieties. However, available information indicated that bitter almond varieties are not grown in commercial almond orchards. Furthermore, although the use of bitter almonds in almond drinks cannot be completely ruled out, based on the information supplied by industry, the Committee was satisfied that it was extremely unlikely that bitter almonds would be used in the production of almond drinks. Overall, Members agreed that, based on exposure from sweet almonds, there were no specific concerns for acute toxicity from cyanogenic compounds in almond drinks.

56. Members asked if roasted or unroasted almond nuts were used to make almond drinks as this affected the potential AFB1 content. It was explained that both roasted and unroasted almond nuts were used. It was agreed that this should be stated throughout the statement.

57. Members agreed that a section on the allergenicity of almond drinks should be included in the statement.

58. Members made a number of additional minor comments on the structure and content of the draft statement.

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

Item 6: Chitins and Chitosan Bio-Based Food Contact Materials (BBFCMs) TOX/2020/42

60. No Interests were declared.

61. In May 2020, a paper entitled "Scoping paper: alternatives to conventional plastics for food & drinks packaging (TOX/2020/24)" was presented to the COT. Due to the diversity of bio-based food contact materials (BBFCMs) available on the market, the Committee agreed that when determining the priorities for review, it would be helpful to focus on the BBFCMs that were most likely to be used in the UK, either directly or through import, as well as those of particular policy concern.

62. Since the FSA's Food Contact Materials (FCM) Policy team have received a number of enquiries on chitin-based BBFCMs and chitosan-based drinking straws regarding their allergenic content, this discussion paper focuses on the immunogenicity and allergenicity of chitin- and chitosan-based BBFCMs.

63. Chitin is the second most abundant polysaccharide on earth after cellulose and can be extracted from the cell walls of fungi, and from the exoskeletons of crustaceans and insects. Chitosan is commonly manufactured from chitin, and is used in some food applications, whilst other chitin-based food products are in development.

64. Paper TOX/2020/42 described the manufacturing process of chitin, where the extent of deproteinisation was reported. Incomplete deproteinisation of chitin may lead to the presence of allergenic proteins, such as tropomyosin, in the final material. Tropomyosin is the main allergenic protein in sea food, which can cause allergic reactions in sensitised individuals. Several studies have reported the immunogenicity of small chitin and chitosan fragments, which may be recognised by the immune system as exogenous and cause an immune response. A case of immediate-type allergy for a chitosan-containing health food has been reported in a 47-year-old patient (Kato et al., 2005)[3], however only the abstract of this publication was available in English.

65. Members considered that the paper provided an overview of the potential hazard but needed to include additional information, such as clearly differentiating between fungal and shellfish sources of chitin, which posed different potential risks. In addition, the possibility of exposure to mycotoxins from fungal derivatives also needed to be addressed. It was noted that chitinase (discussed in paragraph 52 of the discussion paper) was not relevant to the assessment.

66. It was agreed that the risk of allergenicity from chitin- or chitosan-based BBFCMs on the basis of the potential presence of allergenic proteins appeared to be low. However, to confirm this, more information was needed. In particular, additional protein characterisation data for chitosan and the final BBFCMs (against chemical and enzymatic methods of deproteinisation) would be useful. In addition, migration

[3] Kato Y., Yagami A., & Matsunaga K. (2005) A case of anaphylaxis caused by the health food chitosan. Arerugi 54: 1427-1429

and consumption data for BBFCMs were required. Information on the total amount of residual protein (expressed as mg/g BBFCM) would also be helpful in estimating risk.

67. The Committee considered that the potential risks of dermal exposure also needed to be addressed; in this respect, liaison with MHRA for relevant data on wound dressings or similar applications might be helpful. One Member noted that the ED01 for chitin or chitosan was not known; this was the reference dose for crustacean-based proteins that may be appropriate to asses risk of allergenicity, (although the allergen may not be a chitin/chitosan hapten), and furthermore that any data of human allergic reactions to chitin/chitosan in communities where eating edible insects was common would be helpful.

68. The available clinical ingestion data indicate that the immunological properties of chitin and chitosan were of low concern in the context of BBCFMs. For example, there were good data on supplements, where chitin was well tolerated at higher exposure than would be expected from use of BBFCMs. However, it was noted that there were some adverse effects associated with high intakes of the raw materials in clinical studies, which were typically mild symptoms of gastrointestinal tract distress such as diarrhoea, bloating, or vomiting. It was agreed that these adverse effects were not of concern, particularly for BBFCMs as the processing leads to a more inert final material. Furthermore, it was agreed that the phagocytosis of small fragments of chitin or chitosan appeared to be the same as that of similar-sized particles in general.

69. The Committee agreed that the limited information provided in the case report from Kato et al (2005) did not suggest any additional concerns. It was considered that this reported case of immediate-type allergy is most likely due to residuals from the shellfish source from which the chitosan supplement was derived.

Item 7: Review of the implications for risk management based on the EFSA Dioxin opinion TOX/2020/43

70. No interests were declared.

71. Paper TOX/2020/43 reviewed the EFSA 2018 opinion on “Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food”. This opinion was provided by the EFSA panel on Contaminants in the Food Chain (CONTAM panel) and established a new tolerable weekly intake (TWI) of 2 pg TEQ/kg bw, which is 7-fold lower than the previous tolerable daily intake (TDI) of 2 pg WHO-TEQ/kg bw. This change has implications for the UK population, as previously dioxin exposure for most of the population was below a level of concern, whereas exposures, based on the new TWI, could now be at or above a level of concern.

72. PHE noted that moving from the TDI to the TWI would also have consequences on the planning and permit applications for industrial installations, some of which emit dioxins.

73. The Committee had commented on the draft opinion in 2018 and it was concluded that, whilst there was a high degree of uncertainty, the studies used by EFSA could not be dismissed.

74. The Committee noted that the EFSA opinion appeared to be a narrative rather than systematic review, and that there were issues of transparency and robustness with the overall assessment.

75. The Committee questioned the use of the Russian Children's study[4] to derive the new TWI as the Seveso study[5] had reported findings inconsistent with this. Concerns related to the uncertainties in the Russian Children's study included the observation that some of the sperm counts increased with higher concentrations of dioxins; overall the study was generally considered by the Committee to provide only a weak data set. Due to these uncertainties, the committee considered the 7-fold reduction in the TWI as possibly being too conservative.

76. Overall, the human data presented by the CONTAM panel were considered inadequate by themselves as a basis for the TWI. This implies that a further in-depth review of TDI and TWI values, using all of the data from the animal and epidemiological studies, would be necessary.

77. Inconsistencies in the animal dataset presented in the EFSA opinion were also identified. In particular, the selection of the Faqi et al. (1998)[6] study over the Bell et al. (2007a-c) studies[7] to evaluate the critical body burdens obtained from other

[4] Humblet O, Williams PL, Korrick SA, Sergeyev O, Emond C, Birnbaum LS, Burns JS, Altshul L, Patterson DG, Turner WE, Lee MM, Revich B and Hauser R. (2011). Dioxin and Polychlorinated Biphenyl Concentrations in Mother's Serum and the Timing of Pubertal Onset in Sons. Epidemiology, 22, 827-835.

[5] Eskenazi B, Warner M, Marks AR, Samuels S, Needham L, Brambilla P and Mocarelli P. (2010). Serum Dioxin Concentrations and Time to Pregnancy. Epidemiology, 21, 224-231.

[6] Faqi, A.S., Dalsenter, P.R., Merker, H.J. and Chahoud, I. (1998). Reproductive toxicity and tissue concentrations of low doses of 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin in male offspring rats exposed throughout pregnancy and lactation. Toxicology and Applied Pharmacology. 50(2), pp.383-392.

[7]Bell DR, Clode S, Fan MQ, Fernandes A, Foster PMD, Jiang T, Loizou G, MacNicoll A, Miller BG, Rose M, Tran L and White S. (2007a). Relationships between tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), mRNAs, and toxicity in the developing male Wista r(Han) rat. Toxicological Sciences, 99, 591–604.

Bell DR, Clode S, Fan MQ, Fernandes A, Foster PMD, Jiang T, Loizou G, MacNicoll A, Miller BG, Rose M, Tran L and White S. (2007b). Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the developing male Wistar(Han) rat. I: no decrease in epididymal sperm count after a single acute dose. Toxicological Sciences, 99, 214–223.

studies was also questioned. The findings of the Faqi et al. (1998) study were not replicated by the Bell et al. (2007a-c) studies, which were commissioned by the FSA because there were specific concerns about the reliability of the Faqi et al. (1998) study; body burdens were not determined and a no observed adverse effect level had not been identified; however, in the Bell et al. (2007a-c) studies a body burden was determined for the low observed adverse effect level.

78. The Committee commented that, overall, the data presented in EFSA's opinion implied that humans were more sensitive to dioxins than rats. However, if toxicological effects of dioxins were due to interaction with the aryl hydrocarbon receptor (AHR), this was inconsistent with the existing body of data on dioxins and the relative sensitivity of the human and rat AHR.

79. The Committee concluded that they did not agree with the basis on which the CONTAM panel had established a TWI of 2 pg TEQ/kg bw. It was agreed that this should be considered further, possibly with a *de novo* assessment, as the COT might need to decide on the appropriate endpoint based on the overall database on which to establish a TDI or TWI.

80. As the Committee did not agree with the newly established TWI, the Committee was unable to comment on whether the dietary exposures of infants and young children should be compared to the new TWI. The Committee was also unable to determine what other population groups to which a health-based guidance value higher than the TWI might be applicable. The Committee was unable to determine what the critical health endpoint would be if a higher health-based guidance value were to be set for the aforementioned population groups.

81. It was agreed that it was outside the COT's terms of reference to place the various risks associated with exposure to dioxins and dioxin-like PCBs into perspective against the nutritional benefits from food consumption; however, a joint risk-benefit analysis of contaminants in fish had previously been undertaken by a joint COT and Scientific Advisory Committee on Nutrition (SACN) Working Group and could be a way forward for such assessments in the future.

82. The Committee considered that dioxins would be a useful example to test the framework being produced by the COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence (SETE) subgroup to integrate the evidence in an entire database of toxicological and epidemiological data due to the complexity of the dataset present in the EFSA opinion.

Bell DR, Clode S, Fan MQ, Fernandes A, Foster PMD, Jiang T, Loizou G, MacNicoll A, Miller BG, Rose M, Tran L and White S. (2007c). Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the developing male Wistar(Han) rat. II:chronic dosing causes developmental delay. Toxicological Sciences, 99, 224–233.

Item 8: Additional data on the potential risks from combined exposure to mycotoxins. TOX/2020/44

83. Dr David Lovell declared that he would be involved in the T2 and HT2 review as part of the Joint Food and Agriculture Organisation/World Health Organisation Expert Committee on Food Additives.

84. No other additional interests were declared

85. A preliminary scoping paper regarding the potential risks from combined dietary exposure to mycotoxins (TOX/2020/34) had been presented to the COT in July 2020. Following discussions, the Committee asked the Secretariat to perform a literature search on the availability of biomonitoring data for multiple mycotoxin exposures specific to the United Kingdom (UK) population. Members also requested that information on the mode of action of the reviewed single mycotoxins was included in the summary table, to establish whether any of them could be grouped based on their toxicological effects.

86. Paper TOX/2020/44 comprised two papers presenting the additional data: Annex A reviewed the biomonitoring data and Annex B contained the updated single mycotoxin table.

87. Members highlighted that the reported BIOMIN co-occurrence data related to mycotoxins in animal feed, and thus the use of these data in exposure assessment exercises was likely to overestimate intakes for food consumers.

88. The Committee noted that there was a lack of UK data, particularly in biomonitoring; however, there were a number of studies ongoing. The PHE Secretariat informed members that the UK will not be collecting new data for mycotoxins under the HBM4EU initiative. However, in the future, more data could be obtained through Health Protection Research Units. Such research was considered to be a priority by the COT.

89. Members noted the usefulness of the compiled data which brought together the toxicological endpoints and the mode of action (MOA) of the reviewed mycotoxins in Annex B. Members observed that there were a number of mycotoxins with MOAs involving ribosomal protein synthesis inhibition; however, there was a lack of information on possible additive toxicity.

90. Members recommended as a pragmatic first step that a review should be carried out of the compounds which appeared to show a common effect on protein synthesis, assuming dose additivity, to determine whether there was any potential concern from co-exposure to these mycotoxins.

91. Research is needed on mycotoxins affecting ribosomal protein synthesis to determine whether they do exhibit dose additivity in their effects, to help develop a reliable basis for their cumulative risk assessment.

Item 9: COT Contribution to SACN review of the effects of diet on maternal health: proposed scope of work and timetable. TOX/2020/45

92. No interests were declared

93. The SACN last considered maternal diet and nutrition in relation to offspring health in its reports on 'The influence of maternal, fetal and child nutrition on the development of chronic disease in later life' (SACN, 2011a) and on 'Feeding in the first year of life' (SACN, 2018). In the latter report, the impact of breastfeeding on maternal health was also considered. In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery.

94. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete relevant risk assessments e.g. in the area of food safety advice.

95. This subject was discussed during horizon scanning in January 2020 with a scoping paper being presented to the Committee in July 2020. This included background information on a provisional list of chemicals proposed by SACN. At that meeting, further detail on the terms of reference and choice of chemicals to be considered were requested by Members. Paper TOX/2020/45 seeks to address these requests.

96. It was noted that the provisional list of chemicals was subject to change following discussion by COT who would be guiding the toxicological risk assessment process: candidate chemicals or chemical classes can be added or removed as the COT considered appropriate. Paper TOX/2020/45 sought to clarify the terms of reference for the project so that the Committee could decide on priorities, chemicals to omit or add, and those that could be combined into overarching statements.

97. Paper TOX/2020/45 set out the endpoints from those that SACN had chosen to review and which might be considered as being potentially toxicological in nature, and hence of interest to the COT; however, the Committee decided that this was not its usual way of assessing chemical risk. Rather than start from a list of endpoints, the COT would need to consider whether any relevant endpoint could not be assessed.

98. To start the project, and pending further consideration, papers on iodine and vitamin D had been prioritised. The Committee was asked, in the light of recent publications in the literature, whether caffeine should also be considered as a priority, but it was decided that it could be of lower priority because of the uncertainties in its toxicological database. Vitamin A (retinol) was also considered to be low priority as it was subject to existing advice that retinol supplements and foods such as liver should be avoided during pregnancy.

99. The Committee agreed that mycotoxins should be a priority, as well as resveratrol, since there had been little consideration of it as a supplement. It would also be useful to consider what other supplements might be taken by pregnant women. Other substances that could be added to the list for review were

phytoestrogens and other estrogenic substances, phthalates, and perfluoroalkyl compounds (e.g. PFOS, PFOA).

100. Members decided that compounds could be grouped into an overarching statement on the basis of their chemical properties, although those for which large databases of information were available should be presented as single papers.

101. Since the Committee was considering dioxins separately, these would be considered once conclusions had been drawn regarding the newly proposed EFSA TWI for those compounds; this would include any risk -benefit analysis of fish consumption that was needed.

102. It was agreed that the selected compounds would be triaged on the basis of exposure and toxicity, and the Committee would be assisted in their deliberations by a Table of information to this effect.

Item 10: Development of COT guidance (reserved). TOX/2020/46

103. On the 1st January 2021, the transition period following the United Kingdom (UK) leaving the European Union (EU) will have ended and the UK will then be undertaking the risk assessments of regulated products that would have previously been done by EFSA. Three Joint Expert Groups (JEGs) have been established to do this work – the three JEGs cover animal feed and feed additives, food contact materials, and food additives, enzymes and other regulated products and are overseen by their parent SACs - COT, the Advisory Committee on the Microbiological Safety of Food (ACMSF) and the Advisory Committee on Animal Feedingstuffs (ACAF)

104. Guidance will be needed for applicants in the future and this is the subject discussed in this paper. This item was discussed as reserved business and the minutes will be published in due course

Item 11: COT Terms of Reference and Code of Practice – 2nd draft revision. TOX/2020/47

105. The FSA Board is trying to encourage greater consistency among the different FSA Scientific Advisory Committees (SACs) in their Terms of Reference (ToR) and Codes of Practice (CoP). A template has been developed by the Chief Scientific Advisors Team and the FSA Science Council, and the current COT ToR and CoP have been revised to follow the common format. In general, the same information is included as in the previous ToR, but the order in which it has been presented has been revised.

106. However, the COT is different to the other FSA SACs in that it is one of three sister Committees, along with COC and COM, which are jointly sponsored by the FSA and DHSC. Therefore, any changes will also need to be acceptable to these Committees and to DHSC. The COC and COM will be considering this topic at their

Autumn meetings, and further changes may be needed following their discussions along with any changes arising from the restructuring of PHE.

107. The text used in paper TOX/2020/47 was based on that published in the annexes to the COT/C/M Annual Report, however, some of the same information is also on the COT website.

108. A revised version of the ToR and the CoP was discussed in the May 2020 COT meeting. A number of suggestions were made by Members and were reflected in the revised text.

109. Members agreed that the role of the lay members as reflecting the view of the general public should be made clearer. It was also agreed that the role of the Assessor should be reworded to distinguish it from that of Government officials with an interest in particular items. In the section on the "Functions of the Secretariat" the mention of how Committee advice is used should be further clarified.

110. It was agreed that the relationship between the DHSC and PHE should be explained. The role of individuals who provided SACN and Science Council liaison also needs to be captured.

111. It was noted that the definitions of non-specific and non-personal interests were unclear, and the provision of examples could be helpful. Clarity was also needed on recording the interests of close family Members.

112. A number of additional suggestions for minor alterations to the text were made, such as the ordering of some of the headings for clarity.

113. It was agreed that, subject to the outcome of COC and COM discussions, the paper could be cleared by Chair's action.

Item 12: Update on the work of other advisory committees and AOB. TOX/2020/48

114. The papers on the work of other SACs was provided for information.

Item 13: Any other business

115. A Member recalled that a workshop on the microbiome had previously been planned for 2019 but had to be cancelled, and requested that further consideration be given to holding such a workshop in due course.

Date of next meeting

116. The next meeting of the Committee Meeting will be at 10:00 on 27th October via Skype and TEAMs.