CC/MIN/2017/02

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Minutes of the meeting held at 10.30am on Thursday 20th July 2017 at Department of Health, Skipton House, 80 London Road, Elephant and Castle, London, SE1 6LH.

Present

Chair:	Professor D Harrison	
Members:	Mr D Bodey	
	Dr G Clare	
	Dr J Doe	
	Professor R Kemp	
	Dr D Lovell	
	Professor N Pearce	(Items 1-5)
	Dr L Rushton	
	Professor H Wallace	
	Dr R Waring	
	Professor S Warnakulasuriya	
Secretariat:	Miss B Gadeberg	PHE Scientific Secretary
	Ms C Mulholland	FSA
Assessors:	Ms L Lawton	Defra
	Dr H McGarry	HSE
	Mr N O'Brien	VMD
	Dr O Sepai	PHE

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ITEM 1: Apologies for absence and announcements

1. Apologies were received from Drs C Powell and P Greaves, Dr Gott (FSA Secretariat) who was represented by Ms Mulholland, and Assessors Dr Henry Stemplewski (MHRA), Dr Colin Ramsay (Health Protection Scotland), Mr Ian Martin (EA), Dr Jacqui McElhinney and Dr Will Munro (Food Standards Scotland). Dr Steve Morris and Dr Penny Carmichael (Defra) sent apologies and were represented by Ms Lawton.

2. Members were reminded to declare any interests they may have in an item before its discussion.

3. The Committee had in early 2016 been informed of the review of attendance and reading fees by DH. It was noted that Members reappointed as of 1st June 2016 would no longer receive attendance and reading fees from 31st May 2017 in accordance with their reappointment letters, unless there were exceptional circumstances. Members still receiving fees and all Members claiming expenses needed to submit claim forms and return these to Natalie Blowfield, COC Administrative Secretary.

ITEM 2: Minutes of meeting held on 23rd March 2017 (CC/MIN/2017/01)

4. Only one typographical amendment was made to the March 2017 minutes.

ITEM 3: Matters arising

Item 5: Synthesising Epidemiological Evidence subgroup – draft report (CC/2017/02)

5. Following the COC meeting in March, the Synthesising Epidemiological Evidence subgroup (SEES) reports were reviewed by the COT. The COT had requested that some minor changes be made to the report and for the following actions to be undertaken:

- The COT agreed that the one of the recommendations “A designated individual representing government advisory committees should have continued contact with international methodological initiatives (e.g. the Cochrane collaboration policy group, RISK21 group) and that resources are made available for this, including attendance at key meetings” should be brought to the attention of the Food Standards Agency’s Chief Scientific Advisor and the Chief Medical Officer.

- With regard to epidemiology training for the secretariat and new COT Members, the COT were informed that the Interdepartmental Group on Health Risks from Chemicals (IGHRC) currently had no plans to repeat this course in the future due to funding constraints. The COT Secretariat would bring this to the attention of the IGHRC Secretariat and also look into other options.

- With respect to “further work on combining epidemiological and toxicological evidence and understanding of cross-design synthesis studies” the COT concluded that since the recommendations would need to be considered by the FSA, the Chairs of the COC and the COT would write and bring the

recommendations to the attention of the FSA's Chief Scientific Advisor and the Chief Medical Officer.

- The document would be finalised with input from the COC and COT and then circulated to other committees and the IGHRC. The COT agreed that this report would be of benefit to a wider range of people and organisations. The Committee recommended that the report should also be published in the scientific literature. It was agreed that the subgroup should aim for submission in the summer.

6. The SEES subgroup Secretariat and Dr Hansell would be meeting on the 26th July to discuss the completion of the report, for distribution to other Committees, and preparation of a manuscript for publication.

7. The Committee noted that the document would form a useful part of induction to the working of the COC, in addition to sitting as part of Guidance Statement G02 on "Interpretation of Evidence of Carcinogenicity in Humans: Epidemiology and Case Reports".

Item 6b: Draft updated General Introduction to G07 Alternatives to the 2-year Bioassay (CC/2017/04)

8. This document had been amended, and would be cleared by Chair's action, along with parts C and D, when part C, to be discussed as part of this meeting agenda, was agreed by the Committee.

Item 7: OECD guidelines: Standard Project Submission Form for the ToxTracker assay (CC/2017/06)

9. The Committees comments on this assay had been provided to the co-ordinators of the UK response to the submission.

Item 9: Follow up discussion of horizon scanning topics (CC/2017/08)

10. It had been agreed at the March meeting that a scoping paper on nanomaterials should be brought to the present meeting, but this had as yet not been progressed. There would be an update from Defra on nanomaterials under any other business at this meeting and then it would be raised at the joint COC, COM and COT horizon scanning session in October.

Item 10: 2016 Annual report contribution

11. This had been cleared by the Chair and it was expected that the Joint COT, COM and COC Annual report would be published on 21st July 2017. The Secretariat was working on getting website statistics to use as feedback on use of Committee advice.

ITEM 4: Second draft statement on possible carcinogenic hazard to consumers from Insulin-like growth factor-1 (IGF-I) in the diet (CC/2017/10)

12. No interests were declared for this item.

13. This paper presented a non-technical summary to the statement, along with a revised version of the statement for discussion. A tabled paper had been provided which contained updated data tables from the back of the draft statement following further checking.

14. The main amendments to the paper since the draft reviewed in March were updated exposure data, and the original reference providing information on endogenous IGF-I production had been identified.

15. With respect to the non-technical summary, a number of suggestions for amendment were made, and it was agreed that focus should be on the main messages to take from the statement. It was agreed that the public interest representatives would work with the Secretariat to amend the non-technical summary, before circulation to all Members for comment and then agreement by Chair's action.

16. For the main statement, it was queried whether an Ames test had been carried out. The statement would be reviewed to ensure it was clear when studies were considering circulating IGF-I or dietary IGF-I, to appropriately support the conclusions about IGF-I in the diet.

17. Comments were also requested from Members by correspondence on the data tables provided in the tabled paper.

ITEM 5: Guidance statements

18. Professor Heather Wallace declared that she had been appointed as the Chair of a new European Food Safety Authority (EFSA) working group on the Threshold of Toxicological Concern.

Item 5a) Discussion of presentation of Guidance statement series

19. With the guidance statement series nearing completion, as number of aspects were briefly discussed. It was agreed that non-technical summaries would not be produced for each guidance statement, as the General Introduction would cover the whole series.

20. The Committee would also adopt the approach of using a version number (X.1) for minor updates to any document, but full revisions would give a new version number (X+1.0).

21. Finally it was noted that some of the statements did not as yet include the cover sheets present on the newer documents. These would be added as the revisions go forward.

Item 5b) Revised draft General Introduction to the Guidance Statement series (CC/2017/11)

22. This paper presented a revised draft of the General Introduction to the guidance statement series following discussion in March.

23. A number of comments were made on the revised draft. It was agreed that the amendments would be incorporated in the document and then circulated to Members for agreement prior to approval.

24. It was noted that a glossary document covering all the statements would also be prepared.

Item 5c) Second draft of COC Guidance statement COC/G07: Part c) Omics, high-throughput screening, and bioinformatics (CC/2017/12)

25. This paper presented a second draft of this part of the guidance statement on alternatives to the two-year bioassay.

26. It was agreed that the Chair would consider this statement particularly with reference to big data approaches and revise the document accordingly. It would then be circulated for comment by correspondence.

Item 5d) Draft updated COC/G03: Hazard identification and Characterisation: Conduct and interpretation of animal carcinogenicity studies (CC/2017/13)

27. Minor suggestions were made for this draft update to the guidance statement, in particular outlining the difference between genotoxic and non-genotoxic carcinogenicity. It was agreed that the revisions could be made and the document approved by Chair's action.

Item 5e) Draft updated COC/G04: The use of biomarkers in Carcinogenic Risk Assessment (CC/2017/14)

28. This paper presented a draft update on the guidance statement on use of biomarkers.

29. It was agreed that while the updates should reference newer work as appropriate, the list of references should not be extensive as the short updates to the guidance were not a systematic review. It was also noted that distinction should be made for biomarkers which accumulate in the body and those which only provide a measure of current exposure.

Item 5f) Draft updated COC/G05: Defining a point of departure and potency estimates in carcinogenic dose response (CC/2017/15)

30. This paper presented a draft update to this guidance statement and highlighted recent guidance from EFSA on the benchmark dose (BMD) approach and from EFSA and the World Health Organization (WHO) on the threshold of toxicological concern (TTC).

31. The Committee considered it important to fully review the recent developments in the BMD and TTC approaches to provide clear guidance on these topic areas, but this should form part of a substantial revision to the guidance. Such a revision could also link with ongoing work by COM considering quantitative genotoxicity assessment using the BMD approach, in addition to restructuring the order of the document.

32. It was agreed that a short update should be made to the statement in the short term adding a preamble noting the developments in the field and that a full revision of the statement would be undertaken following further detailed review of the recent developments in the BMD and TTC approaches.

ITEM 6: The toxicological evaluation of novel heat-not-burn tobacco products: First draft statement and follow up information from the joint Committee discussion (Reserved business) (CC/2017/16)

33. No interests were declared.

34. This item was discussed in reserved session as it pertains to commercial data.

ITEM 7: Horizon scanning

Papers of Interest

Mutational signatures associated with tobacco smoking in human cancer – and associated editorial paper (CC/2017/17)

41. This paper provided a recent journal paper and associated editorial paper on mutational signatures associated with tobacco smoking. The Committee suggested that this paper could be considered when the guidance statement on biomarkers (G04) undergoes a full version revision.

Alcohol effects on the epigenome in the germline: Role in the inheritance of alcohol-related pathology (CC/2017/18)

42. This paper provided a recent journal paper on inheritance of alcohol effect through the epigenome. The Committee noted that the paper indicated a three generation effect through the male line following *in utero* exposure to alcohol, though these results needed to be reproduced. The paper also highlighted the complexity of such investigations.

Horizon scanning follow up paper (CC/2017/19)

43. This paper presented an update following the discussions of horizon scanning in March 2017.

44. With respect to e-cigarettes it was queried whether COC would conduct any work in parallel with the COT, but it was expected that aspects of relevance would be referred to COC as required. The Secretariat agreed to check whether any of the EU non-food scientific committees had evaluated e-cigarettes.

45. It was suggested that a presentation on adverse outcome pathways (AOPs) would be helpful, and should include a discussion afterwards about the role of AOPs in predicting toxicity and explaining toxicity. The COM's work on N-ethyl-N-nitrosourea might also be of interest.

46. The Committee also agreed to consider the paper by Tomasetti, Li and Vogelstein (2017)[a] as a substantive item along with papers on causal inference at the November meeting.

ITEM 8: Any other business

Whitehall Working Group - Amendment of the REACH Annexes on nanomaterials information requirements

47. The Committee was informed that the Defra chemicals team was setting up a working group to discuss the modification of the REACH Annexes with respect to nanomaterials (NMs) as NMs were not specifically mentioned in the current legal text. The Annexes were being updated to amend this and Defra was seeking cross-Whitehall agreement on the UK negotiating position. A preliminary discussion meeting was being held on 19th July with further meetings to follow. It was highlighted that COC would consider the carcinogenicity of NMs.

Cell transformation assays

48. Through the OECD, the Secretariat had been informed that the origin of the cells used for the Bhas 42 CTA appeared to have become contaminated many years ago. This affected the mechanisms in the assay altering how the cell line can be used and understood. An amendment to the OECD Guidance document was being discussed. This was flagged to the Committee in the context of guidance statement G07 Alternatives to the two-year bioassay part B, which refers to this COM guidance on CTAs.

Secretariat support contact

49. The Committee were informed that the PHE Secretariat support contract, which had previously been provided by Imperial College London, was being negotiated. The Committee would be informed once the contract was in place.

Human biomonitoring for Europe (HBM4EU)

50. PHE are one of the partners on a Horizon 2020 project on human biomonitoring, which links in with the Committee's guidance statement on biomarkers, discussed earlier at the meeting. The Committee were informed for awareness as the time points at which Committee input might be sought on outputs from the project were currently uncertain, but PHE would be keen for input to be obtained where relevant.

ITEM 9: Date of next meeting

51. The date of the next meeting will be the joint Committees meeting on 9th October 2017.

[a] Tomasetti C, Li L, Vogelstein B (2017) Stem cell divisions, somatic mutations, cancer etiology and cancer prevention. Science 355, 1330-1334.