CC/MIN/2021/01

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

Minutes of the meeting held at 10.30 am on Thursday 11th March 2021 by Teams.

Present

Chair:	Professor D Harrison	
Members:	Mr D Bodey	
	Dr G Clare	
	Dr M Cush	
	Dr R Dempsey	
	Dr J Doe	
	Dr R Haworth	
	Dr R Kemp	
	Dr D Lovell	
	Prof N Pearce	(am only)
	Dr L Rushton	
	Dr L Stanley	
	Prof H Wallace	
Secretariat:	Miss B Gadeberg	PHE Scientific Secretary
	Dr D Gott	FSA
	Ms C Mulholland	FSA
Assessors:	Dr H McGarry	HSE
	Mr N O'Brien	VMD
	Dr O Sepai	PHE
Officials:	Dr B Doerr	FSA
	Dr G Drummond	PHE
	Ms S Macchiarulo	PHE
	Dr C McCallion	FSA (Items 9-11)
	Dr L Stewart	PHE
Invited Experts and Contractors:	Dr R Bevan	IEH Consulting
	Dr P Rumsby	IEH Consulting
	Dr K Vassaux	IEH Consulting
Observers:	Professor P Harrison	IEH Consulting
	Professor L Levy	IEH Consulting

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ITEM 1: Announcements and apologies for absence

1. The Chair welcomed Members, and other attendees to the meeting. Apologies were received from Officials: Prof J O'Brien (FSA Science Council) and Dr J McElhiney (FSS).

2. The Committee was informed that this was Dr David Lovell's last meeting as his term as Chair of COM was coming to an end. Dr Lovell was thanked for his contributions to the COC and wished all the best for the future.

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

ITEM 2: Minutes of meeting held on 24th November 2020 (CC/MIN/2020/03)

4. The minutes were agreed with no changes.

ITEM 3: Matters arising

Item 3 Matters Arising – Guidance statement G01 – A strategy for risk assessment of carcinogenicity

5. This document had been published on the COC website.

Item 3 Matters Arising – Guidance statement G08 – Risk assessment of the effect of combined exposures to multiple chemicals on carcinogenicity

6. This document had been published on the COC website.

Item 3 Matters Arising – Draft position paper: The Tumour Microenvironment

7. This document was awaiting final amendments before being finalised by Chair's action.

Item 3 Matters Arising – Cancer Risk Characterisation Methods G06 Update

8. This document was awaiting final amendments before being finalised by Chair's action.

Item 3 Matters Arising – Guidance Statement G05: Carcinogenic dose response: defining points of departure and potency estimates - Third draft revision

9. This document had been published on the COC website.

ITEM 4: Presentation on the Human Biomonitoring for EU (HBM4EU) Project

10. No interests were declared for this item.

11. A brief overview of the HBM4EU project was provided with a focus on guideline value (GV) derivation, to provide background information for item 5. HBM4EU was a large European project that started in 2017, with 29 European countries and Israel as members. It aimed to coordinate collection and interpretation

of human biomonitoring data across Europe to provide policy makers with evidence on which to base policy and to monitor policy interventions.

12. PHE led on this project for the UK, with close links to other government departments and agencies to provide a wider input. The chemicals included in the project were suggested by scientists and regulators at a national level and in consultation with European agencies to understand the policy needs required by the data produced in the project. Two priority lists of chemicals had been developed. Scoping documents were produced to support GV derivation and published on the project website.

13. A large number of human biomonitoring (HBM) samples (mostly urine or blood) had been collected across Europe and the levels of priority chemicals in these would be determined. To date, only occupational samples had been collected in the UK but general population sampling was hoped to be conducted in future projects. Data from these measurements would provide an estimate of integrated internal exposure from all routes and, together with findings from a detailed questionnaire, could be used to show risk factors for exposure. European reference values would be determined from the HBM data to show the distribution of exposure across the European population. Development of HBM GVs would allow the HBM results to be interpreted in terms of health. Although most of the chemicals considered also had validated biomarkers of effect, these were often ~~more~~ difficult to interpret ~~than biomarkers of exposure~~ [RH1] as they weren't generally chemical specific.

ITEM 5: Development of Human Biomonitoring Guidance Values in the HBM4EU Project (CC/2021/01)

14. No interests were declared for this item.

15. HBM programmes can provide essential information for identifying population exposures to chemicals that can be assessed with regards to potential health risks against derived GVs in specific population subgroups or areas. These can be important complements to the conventional sources of information for regulatory chemical risk assessments and for supporting public and occupational health protection policies.

16. There was a diversity in the derivation of health-based guidance values for both the general population and for occupational exposure. The paper presented the framework for the derivation of human biomonitoring GVs proposed by the HBM4EU project (outlined in item 4). In addition, an overview of HBM, a description of current schemes gathering HBM data and four illustrative case studies deriving HBM-GVs on BBzP (benzyl butyl phthalate), Hexamoll® DINCH® (1,2-cyclohexane dicarboxylic acid diisononyl ester), BPA (bisphenol A) and cadmium from the HBM4EU project. The COC was asked to consider whether the framework was robust and applicable and whether UK expert committees could endorse the approach giving reassurance in the derived GVs.

17. The Committee queried whether the absence of biomonitoring data for the UK general population could be a potential issue in applying the HBM4EU GVs. While

general population biomonitoring data had not been collected in the UK under the project, it was emphasised that the HBM4EU GVs by definition can be applied to any population and the absence of UK-specific data in their derivation should not affect the application of the GVs to the UK population.

18. The inclusion of an estimated level of confidence associated with each HBM GV was considered a positive feature of the framework. However, it was suggested that these be more explicitly stated, particularly with regards to confidence in the available toxicokinetic data, which was considered a key parameter to allow estimation of initial exposure levels. COC also considered that more emphasis should be included on the 'snap-shot' nature of many biomonitoring measurements which do not necessarily relate to the full body burden of, for example, POPs, which form repositories in lipid-rich tissues.

19. In considering the robustness of the framework, it was accepted that the estimated level of confidence would vary on a case-by-case basis depending on available data, which should reflect in the use of the GV in different tiers for risk assessment purposes. Of the case studies included in the paper, cadmium, as a known carcinogen, was of most relevance to COC. The methodology employed in the HBM4EU GV derivation was considered appropriate by COC members.

20. It was agreed that the framework was a robust and scientifically valid way to determine HBM GVs, and some suggestions had been made to help make the estimated confidence level be more explicitly stated. Application of the framework to UK HBM data, when it became available, was also encouraged. This paper would also be presented to COT in March 2021 and comments received from both expert committees will be recorded as a summary in the Annual Report to provide a consensus view on the framework and GVs. Following discussion of the paper at COT in March 2021, an update would be brought to the COC meeting in July 2021 under matters arising.

ITEM 6: First Draft Updated COC Guidance Statement on Biomonitoring (G04) (CC/2021/02)

21. No interests were declared for this item.

22. The COC has periodically published guidelines for the evaluation of chemicals for carcinogenicity, including the separation of the overall guidance into individual documents to allow faster revision. This included a separate document addressing Biomonitoring (G04), which was last updated in 2018. As part of the rolling review of all COC guidance statements, this paper presented proposed some amendments and Members were asked to highlight any updates or new areas not currently covered.

23. General comments were received around the re-structuring of text to highlight the specific types of biomarkers being considered and updating of references across the document, including reference to the HBM4EU work (see Items 4&5). A shorter document was favoured, removing some of the older information that was now outdated. During discussion, a number of specific comments were also made

regarding possible amendments and additions to G04. It was agreed that the summary section should be updated to reflect changes made to the main text.

24. Members were asked to send any further specific comments to the Secretariat. It was agreed that a second draft updated guidance statement on biomonitoring would be presented at the meeting in July 2021.

ITEM 7: Updated Scoping Document for New Guidance Statement on Weight of Evidence Approach to Assessing Modification of Cancer Risk (CC/2021/03)

25. No interests were declared for this item.

26. In recent discussions, COC has expressed the aspiration to move away from traditional risk assessment approaches for potential carcinogens, to a more holistic approach encompassing consideration of the effects of chemicals on all stages of cancer development. This paper presented an updated scoping document which had been further developed in light of discussions in November 2020.

27. In discussing the approach, COC concluded that there was currently insufficient information available on all aspects of cancer development and the potential modification of these events by chemicals to facilitate its use by risk assessors. Therefore, the draft scoping document would not be developed into COC guidance at this point. Instead, it was agreed a position paper should be prepared and this would be progressed by convening a small sub-group of members to agree content and scope, which would also include a more appropriate title. A first draft position paper was anticipated to be presented to the Committee in July 2021.

28. As a consequence of agreeing the position paper, members also recommended that COC guidance statements G03 and G07 should now be updated, with the aim of these being discussed at the July 2021 meeting.

ITEM 8: Update to Horizon Scanning – March 2021 (CC/2021/04)

29. No interests were declared for this item.

30. This paper presented the standing update on the Committee's horizon scanning activities, as well as outlining ongoing activities by IARC and the EU Scientific Committees.

31. It was noted that one aspect not explicitly covered in the list of topics was new approach methodologies (NAMs). It was noted that there was activity on this within COT, and the COC would be kept updated on this.

32. It was queried whether the UK having transitioned out of the EU would impact on the COCs workload, in particular in terms of work from the FSA. It was noted that the plan was that routine work on regulated products was not anticipated to affect the COC work, but that work on guidance such as that from COC would be important underpinning to the FSAs approach. It was suggested that it would be helpful to have a placeholder on the horizon scan update for this.

ITEM 9: Draft Report on the Synthesis and Integration of Epidemiological and Toxicological Evidence in Risk Assessments (CC/2021/05)

33. No interests were declared for this item.

34. This paper presented the draft report of the joint COT and COC subgroup on synthesising epidemiological and toxicological evidence (SETE), for the Committees consideration and comment.

35. The Committee considered that the document reflected the COC approach and thinking, and it was an intuitive and well written report. It was suggested that the document be reviewed as there was some repetition through it, and the colour use on the diagrams be revisited to avoid assumptions being made on the basis of use of red and green, as well as for accessibility reasons.

36. The COC comments along with those of COT would be fed back to the subgroup and the COC and COT would be provided with an updated draft report with the worked examples once these were finalised.

ITEM 10: Lay Summary on How Committees Evaluate the Relevance and Reliability of Evidence (CC/2021/06)

37. No interests were declared for this item.

38. A scoping paper on the topic of 'biological relevance and statistical significance' (CC/MUT/2020/03) had been discussed at the joint COC/COM meeting in November 2020. Following these discussions, it was agreed that a 'lay' statement would be produced, covering aspects of how Committees address issues relating to the interplay between statistical analysis and biological (and clinical) relevance.

39. A preliminary draft of the lay document had been prepared and circulated to lay members of the COC, COM and COT for comment. This paper presented a first draft document that had been revised to take into account feedback received from lay Members. The first draft document would also be presented to COT in March 2021, along with a summary of COC discussions and opinions.

40. The Committee commented that it was not very clear in reading the document who the target audience was, nor what purpose it was aiming to achieve. In the current format, the document stood somewhere between a general description to a lay audience of the Committee review process and a technical document commenting on the interplay between biological and statistical aspects of study data. Although the narrative style was considered too technical in places, it was appreciated that some of the concepts, such as the statistical concepts of the 'null hypothesis' and 'p' values, could only be simplified to a certain extent.

41. It was agreed that the document contained relevant and useful information which could be used as a basis to develop two separate documents, addressing: (i) an overall general description of how the expert Committee's review process is conducted, aimed at a lay reader; and (ii) a discussion of the interplay between biological relevance and statistical analysis in the evaluation of evidence, which

would be non-technical but aimed at a more informed audience. The development of the documents was subject to feedback from COT meeting, as well as discussion at COM in due course.

ITEM 11: Reserved Business – FSA Science Council Draft Principles and Guidelines on Third Party Evidence (CC/2021/07)

42. No interests were declared for this item.

43. This paper presented a draft set of principles and guidelines on third party and uncommissioned evidence that had been prepared by the FSA Science Council to support consideration of such evidence, and provide transparency on the ways in which evidence submitted in a non-standard way would be assessed

44. A number of comments were made suggesting clarity around consideration of third party and uncommissioned evidence, and how this might be different to other evidence collected in a standardised manner, e.g. through dossiers or via consultation. It was queried who the document was aimed at, as it was considered the Advisory Committees would know how to consider evidence, and it was noted that it was likely to be an external facing paper to inform how uncommissioned evidence would be used. The Committee was informed that the COC and other Committees could be the recipient of such uncommissioned evidence where FSA or other Government Departments and Agencies had received it and required further assessment of how such evidence sat alongside the existing weight of evidence.

45. It was also suggested that the wording around data cleaning be made clear, especially to avoid any suggestion of data manipulation. This linked to obtaining access to raw data as well as clarity on any processing to generate any images provided.

46. The Committee was thanked for its feedback, which would be taken back to the FSA Science Council.

ITEM 12: COC Annual Report 2020 (CC/2021/08)

47. No interests were declared for this item.

48. The draft annual report for 2020 was presented to the Committee. Members would be reminded to provide their updated declarations of interest after the meeting. No significant comments were made on the draft text so it would be finalised for publication in the joint COT, COM, COC annual report 2020.

ITEM 13: Any other business

49. The Chair and Secretariat had discussed upcoming vacancies and Member reappointments with the Department of Health and Social Care. As a result, a number of Members who were coming to the end of their current terms had been contacted to see if they would stay on. The Chair thanked those who had agreed to do so. It would also give the opportunity to take forward the gap analysis for

Committee expertise discussed at the last meeting in good time for appointing new Members to the Committee.

ITEM 14: Date of next meeting

50. The next meeting would be held on 15th July 2021 by Teams.