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

Minutes of the meeting held at 10.30 am on Thursday 18th November 2021 by Teams.

Present

Chair:	Professor D Harrison	
Members:	Dr G Clare	
	Dr M Cush	
	Dr R Dempsey	
	Dr J Doe	
	Dr R Haworth	
	Prof G Jenkins	
	Dr R Kemp	
	Dr L Stanley	
	Prof H Wallace	
Secretariat:	Miss B Gadeberg	UKHSA Scientific Secretary
	Dr D Gott	FSA
	Ms C Mulholland	FSA
	Dr C Potter	FSA
Assessors:	Dr A Axon	HSE
	Mr N O'Brien	VMD
	Dr O Sepai	UKHSA
Sponsor:	Ms S Peters	DHSC
Invited Experts and Contractors:	Dr R Bevan	IEH Consulting
	Dr S Dean	Imagen, COM Member (Item 4)
	Dr P Rumsby	IEH Consulting
Observers:	Ms Gina Hilton	PETA International Science Consortium Ltd
	Mr Matthew Symington	UKHSA
	Miss Ellie McConachie	HSE
	Dr Carmen Jimenez Antunez	DEFRA

ITEM 1: Announcements and apologies for absence

1. The Chair welcomed Members, and other attendees to the meeting. Apologies were received from Mr Derek Bodey, Prof Neil Pearce and Dr Lesley Rushton, Prof John O'Brien (FSA Science Council), Mr Ian Martin (EA), Ms Georgia Hale (DHSC), Ms Liz Lawton (DEFRA).

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

ITEM 2: Minutes of meeting held on 15th July 2021 (CC/MIN/2021/02)

3. The first draft minutes were agreed with addition of a post meeting note flagging an interest for Dr Gill Clare for item 9 as a Member of the Office for Product Safety and Standards (OPSS) Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS).

ITEM 3: Matters arising

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

4. This document was awaiting publication on the Committee website.

Item 3 Matters Arising – Cancer Risk Characterisation Methods G06 Update

5. This document was awaiting publication on the Committee website.

Item 3 Matters Arising – Updated Scoping Document for New Position paper on Modification of Cancer Risk

6. It was noted that the discussion of this topic had been ongoing for some time but had not progressed to a published COC document. In the meantime, a paper had been published in Toxicology Research, which covered many of the aspects discussed by the Committee (Harrison & Doe (2021) The modification of cancer risk by chemicals. Toxicology Research, 10(4), 800-809). The Committee agreed that the discussions on this topic could be recorded in the Annual Report

Item 4 Draft report on the synthesis and integration of epidemiological and toxicological evidence in risk assessments

7. This report had been published on the COT website, and a link had been added from the COC website. Members were encouraged to disseminate the document and it was noted that this report had also been picked up by EFSA.

Item 5 Second draft revised Guidance Statement (G04): The Use of Biomarkers in Carcinogenic Risk Assessment

8. This guidance statement was expected to be presented to COM in March 2022 and would be finalised after that discussion.

Item 7 First draft updated Guidance Statement (G03): Hazard Identification and Characterisation: Conduct and Interpretation of Animal Carcinogenicity Studies

9. The amendments to this guidance statement were in draft and expected to be circulated to the Committee for final comment after the present meeting, prior to approval by Chair's action.

ITEM 4: Presentation by Steve Dean (COM) – "In vitro high content screening using patient-derived cell models"

10. No interests were declared for this item.

11. The presentation described a personalised treatment for cancer that evaluates potential drug therapies using patient derived cell models. The PredictRx assay utilised a biopsy from patients to derive cells that were screened against 60 drugs to determine sensitivity of the tumour cells. There was a good prediction of clinical response with an 89% positive predictive value and 99% negative predictive value for those tested.

12. Since 2019, with informed consent, the patient derived cells had been stored in a Biobank and a searchable database established. The Biobank had a range of solid tumour types and was being expanded to include hematological tumours. The Biobank and database were a key resource for the evaluation of new drug candidates at all stages of development, including the potential to enhance Phase I, II and III clinical trials.

13. The biobank and database were also seen as a potential resource for cancer research to help gain an understanding of carcinogenicity and mutagenicity. Advantages include high throughput analysis of a range of endpoints and, importantly, the cell models were reliable pre-clinical models with a traceable origin and accompanied by patient histories.

14. Following the presentation, it was noted that this had potential for use as a good example of how in vitro methodology may allow risk assessors to steer away from the use of traditional in vivo study data and allow better understanding of mechanisms in humans. It was recognised however that validation would be key to getting clinical acceptance as a diagnostic tool and acceptance of findings within regulatory submissions.

15. The translatability of the approach, particularly the data side, to establish mechanistic rather than response data was also discussed, and it was noted that Artificial Intelligence platforms may play a key role in interpreting mechanistic data. Benefits of the use of the approach to assess risk were considered to include the high throughput nature, availability of detailed genotypic and phenotypic parameters and a response pathway analysis.

16. Dr Dean was thanked for his presentation.

ITEM 5: Second draft of updated Guidance Statement G07: Alternative approaches to the assessment of potential carcinogenicity of chemicals (CC/2021/15)

17. No interests were declared for this item.

18. This paper presented a second draft updated version of G07 'Alternatives to the 2-year bioassay' amended in line with comments received in July 2021, and represented an interim assessment of alternative tests until it was clearer what methodology/ies would be required for risk assessment of potential carcinogenicity not based on the two-year bioassay.

19. Following discussion, some further suggestions were made to improve the clarity of the document. A name change for G07 was also agreed as 'Alternative approaches to the assessment of potential carcinogenicity of chemicals' to reflect this change in emphasis. It was agreed that the second draft version of G07 would be further updated and circulated to Members for comment by correspondence and subsequent approval by Chair's action.

ITEM 6: Horizon scan 2021 (CC/2021/16)

20. No interests were declared for this item.

21. This paper presented the annual horizon scan for COC, including topics from previous horizon scanning sessions and updates on work of other groups, and outlining the balance of expertise on the Committee.

22. The expertise of the Committee was discussed especially taking into account a number of Members were now in their third term of office. Exposure assessment, in silico approaches and data integration were suggested as areas of expertise that could be required in the future. In addition recruitment of Lay Members would also be important in the near term, to keep up the good quality of those on COC presently. An exit review for Members leaving the COC was suggested. It had been proposed at a meeting of FSA Scientific Advisory Committee Chairs that consideration be made of bringing on scientists earlier in their careers to develop as Committee Members. A table was shown to the Committee with the expertise across Members and a version for COM and COT was requested to be clear on the spread of expertise across the three Committees, along with clarity on the remits of the three Committees. With respect to the template for COC provided in the Annex, it was suggested the sentence in the document about 3Rs was moved to a footnote.

23. The Committee was informed that the Secretariat is looking into the possibility of a joint meeting with COM at the March 2022 meetings, once the agenda for these meetings, as well as the format is clearer.

24. Topics suggested in the meeting included endocrine disruption and the link with carcinogenicity, acknowledging that endocrine disruption is also a COT remit; the impact of chemicals on potential for metastasis or progression of cancer, in particular with respect to the Hallmarks of Cancer and linking to the tumour microenvironment topic COC recently published on; communication of cancer risk

and should COC be involved with this, especially with the move away from a yes/no decision on whether a substance is a carcinogen, and ensuring consistency in describing risks, possibly starting with a landscape review of terminology across a number of Committees (FSA and UKHSA) and led by Lay Members; ensuring appropriate considerations are made to acknowledging diversity in the population especially where there might be differences in risk between different groups.

25. It was suggested to provide more information within the horizon scan follow up papers in the future on topics covered by UK Committees as well as international groups.

ITEM 7: Any other business

Dates for 2022

26. Meeting dates for 2022 (2nd March, 21st July and 17th November) had been circulated to Members as calendar invites. Additionally, the COM meeting on 1st March had also been provided as a holding invite as there was a possibility that a joint meeting might be held across the COM and COC meetings on consecutive days. The Secretariat would keep Members informed in due course.

Use of COC guidance

27. It was queried whether it was possible to gather data on use of COC guidance to provide feedback to the Committee about the value of the different guidance statements. This could be either in the format of statistics on visits on the website pages or as a snapshot survey of use by Government Departments and Agencies.

28. It was also suggested to investigate whether there were areas which Government Departments and Agencies would seek further requests for assessment or guidance from COC.

ITEM 8: Date of next meeting

29. The next meeting would be held on 2nd March 2022.