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

Minutes of the meeting held at 10.30am on Thursday 17th November 2016 at Public Health England, Centre for Radiation, Chemical and Environmental Hazards, Chilton, Oxfordshire, OX11 0RQ.

Present

Chair:	Professor D Harrison	
Members:	Mr D Bodey	
	Dr G Clare	
	Dr P Greaves	
	Professor R Kemp	
	Dr D Lovell	
	Professor N Pearce	
	Dr L Rushton	
	Professor H Wallace	
	Dr R Waring	
	Professor S Warnakulasuriya	
Secretariat:	Miss B Gadeberg	PHE Scientific Secretary
	Ms C Mulholland	FSA
	Dr H Garavini	Toxicology Unit, Imperial College
	Dr K Vassaux	Toxicology Unit, Imperial College
Assessors:	Dr H McGarry	HSE (by teleconference)
	Dr O Sepai	PHE
Observers:	Dr A Mullen	The Dairy Council (Item 4)

ITEM 1: Apologies for absence and announcements

1. Apologies were received from Drs J Doe and C Powell. One member had provided written comments. Dr D Benford (FSA Scientific Secretary) sent apologies and was represented by Ms C Mulholland. Apologies were also received from Drs W Munro (Food Standards Scotland) and H Stemplewski (Medicines and Healthcare products Regulatory Agency), Messrs S Fletcher (Veterinary Medicines Directorate) and I Martin (Environment Agency).

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

ITEM 2: Minutes of meeting held on 21st July 2016 (CC/MIN/2016/02)

3. A change was suggested for paragraph 19, to make clear that the highest tested dose for pharmaceuticals is below the maximum tolerated dose which is used for other chemicals.

ITEM 3: Matters arising

Alcohol – Government response to the consultation

4. The Government response to the consultation on the draft alcohol guidelines had been published and the final wording of the guidelines confirmed; these are available here: https://www.gov.uk/government/consultations/health-risks-from-alcohol-new-guidelines and here: https://www.gov.uk/government/publications/alcohol-consumption-advice-on-low-risk-drinking respectively. A number of changes had been made to the language of the guidelines, but not the guidelines themselves. Following the consultation and further discussion by the Guidelines Development Group, the UK CMOs had not recommended a value for the single occasion drinking guideline.

COT-COC Synthesising epidemiological evidence subgroup

5. The subgroup met on 28th October 2016 to discuss the draft report. It was anticipated that the draft would be ready for review at the March meetings of COT and COC.

ITEM 4: Possible carcinogenic hazard to consumers from Insulin-like Growth Factor-I (IGF-I) in the diet (CC/2016/11)

6. This paper presented information linking dietary exposure, IGF-I levels and cancer risk. Studies investigating diet and IGF-I levels are also discussed in particular intervention studies on supplementation with milk, milk protein or other protein types.

7. It was noted that there were a number of uncertainties in the evidence presented over the time the Committee had been reviewing this topic. Firstly it was still not clear if IGF-I is absorbed intact, the exposure from dietary sources other than milk and how consumption levels and circulating IGF-I levels vary over time. In addition there were some confounders that were not adequately addressed, including how to account for tumours producing IGF-I.

8. The Committee was asked to consider two studies[a], which it was agreed did not raise any concerns. Overall with respect to milk or protein consumption and its effect on circulating IGF-I, there was no convincing evidence of a subsequent effect on cancer risk

9. It was suggested that the evidence be presented in a summary table form to enable easier identification of positive and negative findings. In addition information on dietary contribution to total circulating IGF levels should be presented.

10. It was agreed that a short statement drawing together the Committee's discussion would be prepared for discussion at a future meeting with the papers presented at previous meetings provided as supporting papers at publication.

ITEM 5: Horizon Scanning 2016 (CC/2016/12)

11. This paper presented the annual horizon scan for the Committee, with an update on completed, ongoing and potential new topic areas for consideration.

12. The Committee agreed that the topic of Margin of Exposure for children was considered important. It was queried whether this was also a topic for COT, but as the MOE bandings for carcinogenicity were determined by COC it was agreed this should remain on the workplan. It was also noted there was overlap with the lifetime risk aspects raised in relation to the less-than-lifetime topic discussed at the July 2016 meeting. This could also incorporate relevant aspects from the Cancer Genome Atlas[b].

13. The aspect on genomics was noted to be a very broad area, so the Committee would need to ensure a focussed question was addressed. Mechanisms and particularly non-genotoxic modes and mechanisms of action were ongoing topics of importance for COC. While there was a link to paper CC/2016/14 for discussion at this meeting, there was also a need to continue keeping informed in this area.

14. It was noted that a joint COT, COM and COC workshop incorporating a discussion on epigenetics was planned for autumn 2017, and further information would be provided to the Committee as it became available.

15. The *in vitro* systems available for testing, including 3D models and organs-on-chips, were of continued interest, again overlapping with paper CC/2016/14 and also epigenetics. Likewise the immune effects on cancer susceptibility should also remain on the list of priorities and it was noted there was increasing evidence for the importance of stromal interaction.

16. It was noted that the COM had started to discuss quantification of genotoxicity, and there would likely be a need to cross-link with COC as some of the

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[a] Ma J., et al., 2001, "Milk intake, circulating levels of IGF-1 and risk of colorectal cancer in men", J. Natl. Cancer Inst., 93(17): 1330-1336.
Rinaldi S, et al., 2010, "Serum levels of IGF-I, IGFBP-3 and colorectal cancer risk: results from the EPIC cohort, plus a meta-analysis of prospective studies", Int. J. Cancer, 126(7): 1702-15.

[b] https://cancergenome.nih.gov/

approaches propose linking mutagenic potency with carcinogenic potency. The COM's work in this area was continuing.

17. There was continued interest in a presentation on nanomaterials, and it was suggested that this should focus on aspects within the Committee's remit whether in terms of the application or the endpoint. Concern over possible asbestos-like effects of long and thin nanoparticles was noted, and absorption and persistence would also be important aspects to cover.

18. With respect to e-cigarettes and novel tobacco products, it was noted that these could also link with the topic of early life exposure to cigarettes and the long term risk of cancer. The progress in recent years on type, formulation and also marketing of alternatives to cigarettes, particularly e-cigarettes was noted, and it was agreed this should be on the list of priorities and await a referral of the topics from COT.

19. Following this discussion, it was agreed that the following topics in no specific order were a priority:

- Applicability of Margins of Exposure for exposure of young children
- Mechanisms incorporating genomics and the Cancer Genome Atlas
- Epigenetics
- *In vitro* systems - to be undertaken when resource allows
- Immunological and stromal cell modulations relevant to cancer risk
- Nanomaterials
- E-cigarettes and novel tobacco products, and effect of early life exposure to cigarettes

20. It was agreed that in addition to a formal annual horizon scan, a mechanism would be put in place so there would be time at each meeting for topics to be raised and discussed. In addition it was agreed that the Committee would be kept up to date on upcoming topics for IARC and also publications by the EU Scientific Committees. At the next meeting, the Committee would consider the topics in the list and define the Committee's needs within each area.

ITEM 6: Guidance statement G07: Alternatives to the 2-year Bioassay (CC/2016/13)

21. This paper presented the published parts of the guidance statement on alternatives to the 2-year bioassay and was provided for information. It was noted that the introductory section would need updating so it reflects all the component parts.

Item 6a) G07: Alternatives to the 2-year Bioassay, Part C: Emerging technologies (CC/2016/14)

22. This paper presented an overview of potential applications of toxicogenomics and high-throughput screening technologies to carcinogenicity evaluations, to support drafting of Part C of G07 on emerging technologies.

23. The Committee agreed that it was not possible to make a definitive statement on the emerging technologies and their uses, but it would be useful to have a position to acknowledge them.

24. It was suggested that metabonomics should also be discussed within the document as this was considered likely to have an important role in distinguishing genotoxic and non-genotoxic carcinogens.

25. The Committee agreed to use the term 'omics' within the document rather than 'toxicogenomics' to avoid the suggestion that these are only genomic technologies.

26. It was also noted that with the focus of these technologies on *in vitro* systems, it would be important to be aware of the limitations of these systems and how they reflect human biology. There was also overlap with a number of the topics raised under horizon scanning.

27. It was agreed that a revised paper with draft conclusions would be prepared for further discussion at the March 2017 meeting.

Item 6b) First draft statement of COC/G07: Alternatives to the 2-year Bioassay, Part D: Alternative testing strategies for carcinogens incorporating results from short-term tests (CC/2016/15)

28. This paper presented a first draft of this part of the statement. The Committee discussed the document, focussing particularly on the conclusions. It was agreed that the draft would be revised in light of these discussions and then circulated for comment by correspondence. If agreement is reached by correspondence the document will be finalised by Chair's action.

ITEM 7: Incinerators – discussion of studies investigating health effects from incinerators (Reserved business) (CC/2016/16)

29. This item was discussed in reserved session as it pertains to unpublished research. The minutes will be made available when the research is published.

ITEM 8: Any other business

Meeting of Chairs of DH Advisory Committees and PHE-CRCE Secretariats

37. Regular liaison meetings had been established between the DH Advisory Committees, the PHE-CRCE Acting Director, Dr Jill Meara, the PHE-CRCE Secretariats and the DH sponsors.

38. Aspects of interest raised at the last meeting included:

- greater acknowledgement of membership of policy committees in the Stern review of the REF,
- encouragement for Committee Chairs, Members and Secretariats to publicise the Committee's work at relevant conferences and meetings, and
- a request for Committees to flag up areas where UK is losing out/potentially losing out as a result of Brexit.

ITEM 9: Date of next meeting

39. The date of the next meeting will be 23rd March 2017.