

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)

Contents	Paragraph
Item 1: Apologies for absence and announcements	1
Item 2: Minutes of meeting held on 21 st July 2016 (CC/MIN/2016/02)	3
Item 3: Matters arising	4
Item 4: Possible carcinogenic hazard to consumers from Insulin-like Growth Factor-I (IGF-I) in the diet (CC/2016/11)	6
Item 5: Horizon Scanning 2016 (CC/2016/12)	11
Item 6: Guidance statement G07: Alternatives to the 2-year Bioassay (CC/2016/13)	21
a) G07: Alternatives to the 2-year Bioassay, Part C: Emerging technologies (CC/2016/14)	22
b) 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
Item 7: Incinerators – discussion of studies investigating health effects from incinerators (Reserved business) (CC/2016/16)	29
Item 8: Any other business	37
Item 9: Date of next meeting	39

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

^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/>

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

171 **ITEM 8: Any other business**

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

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

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

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

183 **ITEM 9: Date of next meeting**

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

Draft