

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

4 Minutes of the meeting held at 10.30am on Thursday 21st July 2011 at Department of
 5 Health, Room 102A, Skipton House, Elephant & Castle, London, SE1 6LH.

6 Present

7 Chairman: Professor D Phillips

8 Members: Professor A Boobis
 9 Dr P Carthew
 10 Professor P Farmer
 11 Dr P Greaves
 12 Dr D Lovell
 13 Dr B Miller
 14 Dr C Powell
 15 Professor P Vineis
 16 Dr N Wallis

17 HPA Secretariat: Ms F Pollitt (Scientific Secretary)
 18 Ms S Kennedy (Administrative Secretary)
 19 Mr J Battershill
 20 Dr M Cush
 21 Miss B Gadeberg

22 FSA Secretariat: Dr D Gott

23 In Attendance: Dr J Graves (DH)
 24 Dr K O'Leary (HPA Tox Unit)

25 Assessors: Dr C Pease (Environment Agency)
 26 Dr H Stemplewski (MHRA)
 27 Mr Richard Daniels (Item 4 – Department for Education)

28 Observers: Mr Michael Lees (Item 4)
 29 Dr Ovnair Sepai (HPA)

Contents	Paragraph
Item 1: Apologies/announcements	1
Item 2: Minutes of meeting held on 14 th April 2011 CC/MIN/2011/1	3
Item 3: Matters arising not covered by later agenda items Paper by Wooder and Wright submitted by AMVAC	6
Item 4: Relative Vulnerability of Children to Asbestos compared to Adults (CC/2011/10)	8
Item 5: COC Guidance statements – 3 rd draft of the Overarching Guidance Statement (CC/2011/09)	18
Item 6: Update review of cancer incidence near Municipal Solid Waste Incinerators (CC/2011/12)	25
Item 7: Item for Information: Schutze et al. Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study (CC/2011/11)	28
Item 8: Any other business	29
Item 9: Date of next meeting	31

32 **ITEM 1: Apologies for Absence & Announcements**

33 1. Apologies were received from Dr Carolyn Allen, Mrs Rosie Glazebrook and Dr
34 Lindsay Wright. Apologies were also received from Dr Diane Benford (FSA), who was
35 represented by Dr David Gott, Mr Paul Holley (Department of Health), who was
36 represented by Dr Jonathan Graves, Dr Pip Edwards (HPA) and Mr Andrew Smith
37 (HSE).

38

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

41

42 **ITEM 2: Minutes of meeting held on 25th November 2010 CC/MIN/2010/2**

43 3. A few edits were made to the minutes in paragraphs 8, 14 and 15.3.

44

45 4. For item 3a, it was agreed that though Professor Boobis was not at the meeting, as
46 he had made written comments, his Declaration of Interest should be stated. This
47 was that he was a Member of both the Advisory Committee on Pesticides and of the
48 Toxicology Working Group of the Scientific Panel on Plant Health, Plant Protection
49 Products and their Residues (PPR) of the European Food Safety Authority when
50 dichlorvos was discussed in these committees.

51

52 5. The Chairman stated that it is important to ensure Declarations are correctly
53 recorded and categorised.

54

55 **ITEM 3: Matters arising not covered by later agenda items**

56 **Paper by Wooder and Wright submitted by AMVAC**

57 6. Two Members had reviewed the paper by Wooder and Wright^a, highlighted in
58 correspondence received from AMVAC. This paper was a summary of an earlier
59 paper by Wooder, Wright and King (1977)^b which reported an alkylation study in
60 rats. The study showed that at an estimated dose of 6 µg/rat dichlorvos by inhalation
61 did not cause methylation of guanine.

62

63 7. The study was considered to be well performed but it did not rule out the
64 possibility of methylation occurring at higher doses or following administration by a
65 different route. It was agreed that there was no inconsistency between the results of
66 this study and the conclusion of the COM that dichlorvos should be regarded as an *in*
67 *vivo* mutagen at the site of contact. Therefore it would not be possible to rule out
68 the possibility of genotoxicity as a mechanism for the carcinogenicity seen in studies
69 with dichlorvos.

70

^a Wooder MF and Wright AS (1981). Alkylation of DNA by organophosphorus pesticides. *Acta Pharmacol et Toxicol* 48, suppl V, 51-55.

^b Wooder MF, Wright AS and King LJ (1977). *In vitro* alkylation studies with dichlorvos at practical use concentrations. *Chem-Biol Interactions* 19, 25-46.

71 **ITEM 4. Relative Vulnerability of Children to Asbestos compared to Adults**
72 **(CC/2011/10)**

73 8. A number of declarations of interest were made. Professor Phillips and Professor
74 Vineis declared that they had both appeared as expert witnesses in litigation cases
75 on asbestos. Dr Miller stated that he works for an institute where other members of
76 staff have worked on asbestos and appeared as expert witnesses. Dr Carthew
77 declared that he had a lapsed interest from a previous employment, having worked a
78 long time ago on experimental animal studies on fibres, including asbestos fibres.

79

80 9. It was agreed that the Secretariat would seek advice on the Chairman's role in
81 subsequent discussions but, given that this discussion was focussed on the strategy
82 rather than the technical detail, it was agreed that Professor Phillips could chair this
83 item.

84

85 10. Mr Richard Daniels, an environmental engineer working at Partnerships for
86 Schools, was in attendance as a representative of the DfE for this item. Mr Michael
87 Lees, a member of the "Asbestos in Schools Steering Group", was in attendance as
88 an observer for this item.

89

90 11. The Department for Education (DfE) were seeking advice from the COC on the
91 relative vulnerability of children to asbestos. This request arose from discussions in
92 an independent advisory group called the "Asbestos in Schools Steering Group",
93 which reports to the Department for Education (DfE). The Steering Group aims to
94 promote effective management of asbestos in schools and to contribute to the
95 development of guidance on such management. Members were provided with the
96 terms of reference of this group. DfE subsequently asked DH for a study of the risk of
97 asbestos to children and DH facilitated the DfE's request for advice from the COC.

98

99 12. Members were asked to consider the introductory paper and to advise on the
100 strategy proposed by the Secretariat to facilitate the COC's deliberations on this
101 issue. Members were informed that it was the intention of the Secretariat to bring
102 the topic back to the November COC meeting at the earliest for a full discussion. The
103 Secretariat informed the committee about the Health and Safety Executive's
104 scientific advisory committee, the Working Group on Action to Control Chemicals
105 (WATCH), which advises the Advisory Committee on Toxic Substances (ACTS) and
106 HSE on scientific and technical issues relating to the assessment and control of
107 health risks from chemicals. WATCH had recently examined the risks from low level
108 exposure to asbestos in adults and had produced a statement, which would be
109 provided to Members. A representative from HSE could be invited to talk about
110 WATCH's discussions, as background to the COC discussions at the November
111 meeting.

112

113 13. The strategy proposed by the Secretariat included 1) a review of any
114 epidemiological literature on children exposed to asbestos, 2) a review of data from
115 developing countries where children are occupationally exposed to asbestos and the
116 development of mesothelioma in later life and 3) a review of animal data (if
117 available) on the comparative differences between the effects of juvenile versus
118 adult exposure to asbestos. Members were also informed that there were data

119 available in the literature on the levels of asbestos found in school buildings in the
120 US and Italy and it was hoped that the Secretariat could obtain data for the UK so as
121 to provide an exposure perspective to the discussions. The Secretariat sought advice
122 on whether Members would consider it helpful or necessary to co-opt experts from
123 other fields such as juvenile respiratory physiology or asbestos epidemiology or
124 pathology to aid the discussions. Members were asked if they had any other
125 suggestions for experts or areas of expertise which might help to facilitate the
126 discussion

127

128 14. Members offered a number of suggestions for the strategy. Members
129 commented that it is very difficult to perform a quantitative risk assessment for
130 asbestos fibres. A Member suggested that the Committee should consider an
131 intrinsic hazard assessment by age of childrens' exposure given the differences in
132 lung physiology at different ages. For mesothelioma, a Member commented that it
133 was difficult to obtain good data from animal inhalation studies. The potency of
134 fibres is ranked on the basis of body cavity exposure and there may not be animal
135 studies available in the literature on juvenile exposure to asbestos. In terms of
136 intrinsic vulnerability of children, a review of the US EPA model used for risk
137 assessment of inhalation exposure and the ICPR modelling framework for particle
138 dosimetry was suggested. In terms of mesothelioma, Members were reminded that
139 the earlier one is exposed to asbestos the greater the chance of disease. However, it
140 was questioned whether the susceptibility is the same at all ages or if there is a
141 different susceptibility at a younger age.

142

143 15. The significance of obtaining information on airborne levels of asbestos from UK
144 schools was questioned given that the Committee is addressing the relative
145 vulnerability of children compared to adults. The Secretariat considered that these
146 data would be helpful in providing a perspective on exposure during the discussions.
147 Two relevant reports from schools (one theoretical) might be available at the
148 Institute of Occupational Medicine. These studies had been commissioned by
149 education authorities, and it was not yet clear whether it would be possible for the
150 studies to be released to the COC.

151

152 16. Members suggested that there are a number of studies where lung samples from
153 occupationally exposed workers were analysed for fibre burden. These studies might
154 be helpful in the discussions in terms of exposure, case histories and latency to
155 tumours. Also, there are studies in the literature on para-occupational exposure to
156 asbestos that may be informative. A Member commented that he was aware of
157 Italian studies on para-occupational exposure and could investigate whether these
158 included studies of children. Members were informed of a current study being
159 undertaken by Professor Julian Peto on random samples of collapsed lungs but the
160 purpose of the research was unknown. Studies on environmental exposure to
161 asbestos from Libby, Montana; Turkey; and New Caledonia may also be useful for
162 the COC discussion. Members were informed about a recent study in New Caledonia,
163 where the presence of serpentinite on roads was found to be a major environmental
164 risk factor for mesothelioma.

165

166 17. In addition to expertise in juvenile respiratory physiology and in asbestos,
167 Members also considered that differences in inflammatory cell involvement in the
168 responsiveness to inhaled fibres in children compared to adults would be important
169 to consider and expertise should be sought in this area. Members, Assessors and
170 Observers made a number of suggestions for experts in these areas, and on the
171 epidemiology and pathology of asbestos, who the Secretariat could approach to
172 facilitate the Committee's discussions.

173

174 **ITEM 5: COC Guidance statements – 3rd draft of the Overarching Guidance**
175 **Statement (CC/2011/09)**

176 18. This paper presented a further revised draft of the overarching guidance
177 statement following comments at the April 2011 meeting. A revised version of Figure
178 2 was tabled at the meeting.

179

180 19. In discussion of the risk characterisation of non-thresholded carcinogenicity, it
181 was agreed that, rather than continuing to recommend the determination of a
182 Minimal Risk Level (MRL), a Margin of Exposure (MoE) approach should be used. The
183 MoE was considered to provide a better basis for discussion of the degree of concern
184 there might be about an exposure to a compound, compared to the MRL which
185 incorporated uncertainty factors in the derivation of the level. However, it was
186 pointed out that the MRL approach is useful in situations where it is necessary to
187 derive maximum recommended concentrations of a genotoxic contaminant in
188 environmental media. However, in this scenario, case-by-case discussion would be
189 required to determine a suitable uncertainty factors.

190

191 20. For compounds with a mode of action for carcinogenicity showing a threshold,
192 Members commented that the most sensitive endpoint in the toxicological profile
193 should be selected as a basis for the risk assessment, but that this endpoint may not
194 be carcinogenicity.

195

196 21. There was discussion of the Threshold of Toxicological Concern, which was
197 considered a pragmatic rather than biologically-based approach to assessment. It
198 was agreed that, while it has a role in prioritisation of impurities or unavoidable
199 chemicals (e.g. in food), it was not favoured as a means of providing risk
200 management advice.

201

202 22. With respect to Potency Equivalence Factors, given the uncertainties in potency
203 ranking and that they had been little used for carcinogenic risk assessment, the
204 discussion was substantially shortened.

205

206 23. For future developments, it was agreed that the principles of replacement,
207 refinement and reduction should be emphasised. Additionally, moves to consider
208 systemic exposure of animals in carcinogenicity testing, rather than the administered
209 dose, should also be recognised.

210

211 24. A number of amendments were also made to the text, and it was agreed that a
212 revised version would be circulated before the next meeting for any final comments

213 and then agreement would be sought on the statement at the November 2011
214 meeting.

215

216 **ITEM 6: Update review of Cancer Incidence near Municipal Solid Waste**
217 **Incinerators (CC/2011/12)**

218 25. In the late 1990s, the Committee discussed a study by the Small Area Health
219 Statistics Unit (SAHSU) on cancer incidence near incinerators in Great Britain and
220 published a statement which concluded that *'any potential risk of cancer due to*
221 *residency near to a municipal solid waste incinerator was exceedingly low and*
222 *probably not measurable by the most modern epidemiological techniques.'* During
223 2008 and 2009, the COC reviewed reports and epidemiological investigations of
224 cancer incidence near to municipal solid waste incinerators (MSWI) which were
225 published between 2000 and 2009. A second statement was published, which
226 concluded that *"there is no need to change the advice given in the previous*
227 *statement in 2000, but the situation should be kept under review"*.

228

229 26. Recently, a paper by Viel *et al.* (2010) was brought to the attention of the
230 Secretariat. This reported a positive association between living near a MSWI in
231 Besancon, France and non-Hodgkin's lymphoma (NHL). As municipal waste
232 incineration is an active policy issue, a search was performed for any other newly
233 published studies and 2 additional papers were found. These two studies were based
234 in Italy and Brazil and showed a negative association between living near a MSWI
235 and cancer incidence. Members' views were sought on the three epidemiology
236 studies provided for discussion.

237

238 27. Members commented that the Committee paper provided a good summary of
239 the data. The Committee was reminded that it has previously seen papers on the
240 incinerator in Besancon, France and had noted that, for many years, emissions of
241 PCDDs and PCDFs from this incinerator were reported to be far higher than is
242 currently permitted. The Committee highlighted a number of issues in the Viel paper.
243 These included issues with the methodology including small sample size and poor
244 exposure assessment, lack of control for confounding factors and the difficulties in
245 histological classification of NHLs. The Committee concluded that the evidence
246 provided in the Viel paper was weak overall. A Member commented that, in the
247 Brazilian paper, the reference category was very small and, in the Italian paper,
248 the SIRs were completely flat. Overall, the Committee considered that there was no
249 change in the position given in its previous statement.

250

251 **ITEM 7: Item for Information:**

252 **Schutze et al. Alcohol attributable burden of incidence of cancer in eight European**
253 **countries based on results from prospective cohort study (CC/2011/11)**

254 28. At the last meeting, Members expressed an interest in seeing this recent
255 publication from EPIC on the alcohol attributable burden of cancer incidence in 8
256 European countries. A Member commented that the paper is of good quality
257 because it reports the results of a large study with a relatively good exposure
258 assessment and stable estimates. The paper found that 10% of total male cancers

259 and 3 % of total female cancers were attributable to current or former alcohol
260 consumption. The strong statement in the conclusion section of the paper was
261 included to emphasize the public health message on alcohol; it was not a suggestion
262 that there was a threshold for the cancer effects. Members were also made aware of
263 another recent publication from a French group which found that current alcohol
264 consumption guidelines are inadequate for the prevention of cancer and that there
265 was no safe level of alcohol consumption. The COC has carried out reviews in the
266 past on alcohol and breast cancer. A meta-analysis by the Department of
267 Epidemiology and Public Health at Imperial College London showed an increased risk
268 of breast cancer. Similar results were observed by the Oxford Collaborative Group on
269 Hormonal Factors in Breast Cancer. It was suggested that the Committee should
270 issue a statement again in light of the recent publications, to make its position clear.

271

272 **ITEM 8: Any other business**

273 29. Members were informed of a consultation on the future of the DEFRA Advisory
274 Committee on Hazardous Substances (ACHS). The consultation covered the proposed
275 abolition of the ACHS as a statutory Non Departmental Public Body; and on the
276 Government's preferred option to simultaneously reconstitute this body as a new
277 expert scientific committee. The suggested terms of reference for this Committee
278 were also provided. There is concern that the suggested remit of the ACHS contains
279 considerable overlap with that of the COT/COC/COM as the terms of reference
280 include:

281 *"To advise officials, UK Ministers, and other relevant bodies, on request or*
282 *otherwise:*

283 *- on matters of relevance at a domestic, European and global level,*
284 *relating to the protection of the environment, and human health via the*
285 *environment, from potentially hazardous substances and articles,*
286 *including nanomaterials; including on future issues of concern, on impacts*
287 *and on wider strategic linkages;"*
288

289 30. The Secretariat sought the views of Members on the consultation and
290 particularly the revised terms of reference in order to compile a response from the
291 Committee. The Committee were reminded that, while previously the ACHS had
292 given advice on human health, it had not been stated as its role within the existing
293 ACHS terms of reference. In general, the Committee considered that the significant
294 overlap in remit could lead to conflicting messages being given to Ministers and the
295 public. This would not be helpful to Government. The Committee recommended that
296 a joint response from COC/COM/COT would be advisable.

297

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

299 31. The date of the next meeting is scheduled for 17th November 2011 at the
300 Department of Health, Skipton House, Elephant & Castle, London, SE1 6LH. It was
301 noted that it might be necessary to change the date of the meeting and the
302 Secretariat would contact Members in due course.