

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

4 Minutes of the meeting held at 10.30am on Thursday 20 November 2008 at
 5 Department of Health, Room 136B, Skipton House, 80 London Road, Elephant
 6 and Castle, London SE1 6LH.

7 Present

8 Chairman: Professor D Phillips

9 Members: Dr C Allen
 10 Professor A Boobis
 11 Dr P Carthew
 12 Professor P Farmer
 13 Mrs R Glazebrook
 14 Ms D Howel
 15 Dr B Miller
 16 Professor D Shuker
 17 Dr N Wallis

18 HPA Secretariat: Ms F Pollitt (Scientific Secretary)
 19 Ms S Kennedy (Administrative Secretary)
 20 Dr D Mason (Minutes)
 21 Mr J Battershill

22 FSA Secretariat: Dr D Benford (Scientific Secretary)

23 In Attendance: Dr K Burnett (DH Tox Unit, item 6.1)
 24 Dr K O'Leary (DH Tox Unit, items 4, 6.2 & 8)

25 Assessors: Dr A Gowers (EA)
 26 Dr D Gray (HSE)
 27 Mr S Samuels (PSD)

28 Observers: None

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

31 1. Apologies were received from Mr H Brunt (NPHS Wales), Dr S Dyer
32 (DH), Professor D Harrison, Professor R Roberts, Dr H Stemplewski (MHRA)
33 and Professor P Vineis.

34 Announcements

35 2. The Chairman noted that the following members retired at the end of
36 March 2009 and that, therefore, this was their last meeting: Professor D
37 Harrison, Ms D Howell, Professor R Roberts and Professor D Shuker. He
38 thanked them for their work for the committee over the last 9 years.

39 3. The Chairman welcomed Mr J Battershill, Dr K Burnett, Dr D Mason
40 and Dr K O'Leary to the meeting and explained that Prof C Blakemore,
41 Chairman of the FSA's General Advisory Committee on Science (GACS), was
42 expected to join the meeting as an observer [Post meeting: Professor
43 Blakemore was unable to attend the meeting].

44 4. Members were reminded of the need to declare any relevant interests
45 before discussion of items.

46 **ITEM 2: Minutes of meeting held on 17 July 2008 (CC/MIN/08/2)**

47 5. The omission of Dr B Miller from the list of Members present and the
48 incorrect spelling of Ms B Gadeberg's name (line 35) were acknowledged.

49 Line 133: It was highlighted that carcinogenicity studies are not used
50 for risk assessment by COC but are used to identify cancer as an
51 endpoint

52 Line 241: this should refer to letters (b) and (c), not (ii) and (iii)

53 Line 292: "from 18 months" should be inserted after "2 years"

54 Line 327: "would" to be replaced with "should"

55 Line 359: "was" to be replaced with "should be"

56 Line 408: "predictably lead" to be replaced with "would be predicted to
57 lead"

58 Line 453: "which is not a genotoxin" should be inserted after
59 "hexachlorobenzene (HCB)"

60 Line 460: "definitie" to be replaced with "definite"

61 Line 511: "in situations where" to be replaced with "because"

62 Line 512: insert "some of" before "the PAs"

63 Line 531: insert "(STS)" after "soft tissue sarcoma"

64 Line 408: "carrid" to be replaced with "carried"

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

66 6. No matters arising.

67 **ITEM 4: First Update Statement on the Review of Cancer Incidence Near**
68 **Municipal Solid Waste Incinerators (MSWIs) - CC/08/16**

69 7. The Committee were presented with a first draft update statement
70 (CC/07/16) and with a new pre-publication paper by Viel *et al.* (Environ.
71 Health, *paper in press*: doi:10.1186/1476-069X-7-51) which reported further
72 evidence of a link between NHL incidence and exposure to dioxins emitted by
73 MSWIs. Members were asked to review the draft statement and to provide
74 their views on the new paper.

75 8. Members discussed the issue of extrapolation of risk from the levels
76 of emissions during the exposure period in the reviewed studies, to the current
77 level of emissions from incinerators. Since some of the earlier studies
78 showed a positive association between incinerators and cancer risk, it was
79 considered that whilst reductions in exposure would reduce the level of
80 concern, this would not mean there was no potential concern. Members
81 noted that there was a substantial reduction in emissions since the 1980s and
82 asked for the values given in the studies to be put in the context of current
83 emission levels (if available), rather than regulatory limits. Also, more data
84 should be included on some of the studies e.g. whether the study examined
85 emissions from MSWIs only or from other types of incinerator also.

86 9. The committee again reviewed the odds ratio quoted in the study by
87 Zambon *et al* (2007, Environ Health, 6(19)) and decided that their previous
88 comment “the strength of association was poor” was not justified. Members
89 suggested that the comment was removed from the statement, and added
90 that this study provides some evidence for an association with living near that
91 incinerator during the period from 1960 to 1996. The Committee noted that
92 the incinerator emissions during this period were likely to have been higher
93 than current incinerator emission levels.

94 10. Members commented that the tabled Viel paper seemed to take a
95 broadly similar approach to previous papers, although it appeared to have
96 employed a case-control study design. It was agreed that Members would
97 review this paper after the meeting and provide comments to the Secretariat.
98 A paragraph would then be drafted for inclusion into the statement. A new
99 reference in the Viel paper was noted that had not previously been reviewed
100 by the Committee (Biggeri and Catelan. Epidemiol Prev. 29(3-4):156-9,
101 *English abstract, article in Italian*). It was unclear whether this was a
102 municipal, industrial or hazardous waste incinerator; the Secretariat agreed to
103 investigate further.

104 11. Regarding the concluding paragraph, Members requested this be
105 revised to state that extrapolation from previous exposure to the current
106 exposure levels is difficult. A clarification of which ‘certain’ cancers were
107 increased in incidence was requested, since it was relatively reassuring that
108 these did not include common tumour sites, such as the breast. It was also
109 noted that epidemiology studies would be unlikely to be sufficiently powered to
110 detect effects at the current low exposure levels.

111 12. A summary of UK incinerator information was considered appropriate,
112 since this would increase the usefulness of the document to the general
113 public. A good example was noted in the tabled Viel paper, which summarised
114 the French situation. It was also suggested that some advantages to the use
115 of incinerators should be noted, such as generation of electricity from waste.

116 In addition, Members requested some specific editorial changes and
117 requested a list of abbreviations. It was also suggested that the statement
118 should include a link to a website detailing the locations of incinerators in the
119 UK and an indication of who was responsible for monitoring.

120 13. Since this statement is a reiteration of the conclusions of the previous
121 statement and there is a policy need for urgent publication, it was considered
122 appropriate to complete the drafting by e-mail consultation, with clearance by
123 Chairman's action.

124 **ITEM 5: Horizon Scanning - CC/08/17**

125 14. Professor Boobis declared a personal specific interest in hair dyes so
126 was excluded from the discussion on that item. Dr Miller declared a non-
127 personal specific interest for carbon nanotubes, since his institute is involved
128 in research on this subject. It was decided that this should be noted but that
129 Dr Miller should be able to participate in the discussion.

130 15. The Chairman explained that the discussion should not be limited to
131 the items covered in paper CC/08/17 and that additional issues could be
132 raised during the discussion, or indeed at any time during the year. He
133 proposed that each of the topics in the paper be discussed initially, assigning
134 priorities at the end of the discussion.

135 *Possible Carcinogenic Hazard from Dietary IGF-1*

136 16. The FSA Secretariat asked Members whether they wished to consider
137 the possibility that dairy products from recombinant BST-treated cows might
138 increase the risk of cancer in consumers due to elevated concentrations of the
139 insulin-like growth factor IGF-1 in milk. This possibility was raised in a book
140 written by Professor Jane Plant entitled "Your Life in Your Hands".

141 17. Members asked for clarification of whether milk and dairy products
142 from animals treated with BST were allowed to be imported into the EU. The
143 FSA Secretariat explained that dairy products could be imported from certain
144 countries, such as USA and Mexico, that do use BST; furthermore, dairy
145 products from a larger range of countries could be present in processed
146 foods, such as sweets.

147 18. It was considered likely that BST would be subject to proteolysis in
148 the gut. The Committee was aware of advice given by some health care
149 professionals that women with breast cancer should avoid dairy products.
150 Members observed that the concerns relating to dairy products and cancer
151 risk are broader than just IGF-1. It was suggested that the Secretariat should
152 examine the evidence presented in Professor Plant's book and that, if
153 adequate data are presented, these might be brought to the Committee for
154 review.

155 *RNA Related Effects as Mechanism of Carcinogenicity*

156 19. The Committee was presented with a review by Scholzová *et al.*
157 (2007, Cancer Lett. 246(1-2):12-23) on RNA regulation and cancer
158 development. Members considered this to be an area of interest and
159 highlighted research that suggests that microRNAs might play a part in

160 interspecies differences in responses to peroxisome proliferators. There is
161 also evidence that micro RNAs are up-regulated in tumours and have
162 implications more generally for the carcinogenic process. The role of
163 endogenous short interfering RNA species is less clear. The Chairman
164 questioned whether the time was right to review this field. Members
165 considered there to be a substantial amount of emerging data.

166 *Carcinogenic Risk Posed by Carbon Nanotubes*

167 20. A pilot study has shown carbon nanotubes to cause asbestos like
168 (length dependent) pathology in the mesothelium when injected into the
169 abdominal cavity of mice (Poland et al., 2008, Nat Nanotechnol. 3(7):423-8).
170 Members noted that there is considerable debate over the validity of the
171 models used in such studies, the route of exposure and the high doses used.
172 This was considered to be an area that is worth investigating further and
173 Members were keen to hear a presentation on the subject.

174 *Endogenous DNA Adducts*

175 21. The Committee was asked to consider whether it would be
176 appropriate to review the implications of there being a background level of
177 adducts caused by endogenous chemicals for the carcinogenic risk
178 assessment of exogenous chemicals causing the same adduct.

179 22. Members discussed examples of background levels of DNA damage
180 and whether this provides evidence of biological thresholds. It was noted that
181 some regulatory authorities consider that, rather than exogenous exposures
182 being lost in a background of DNA damage, DNA damage resulting from
183 exogenous exposures is added to the background; therefore, there is no
184 threshold. Members noted that human DNA is polymorphic and highly
185 variable and that, whilst the average level of DNA damage in the genome may
186 be increased, this is not necessarily the case for specific genes. This area is
187 still not well understood. It was noted that the COM expects to receive a
188 presentation on this item at its February meeting, and that COC Members
189 were welcome to attend.

190 *Cupric Gluconate*

191 23. A Member had highlighted a recent publication by Abe *et al.* (2008,
192 Arch Toxicol. 82(8):563-71) which presented a medium-term liver
193 carcinogenicity bioassay showing promotion at a Cu dose of about 60mg/kg
194 bw/day from copper gluconate. The Committee did not consider this was a
195 cause for concern, as human exposure to cupric gluconate is well below the
196 level found to promote tumours.

197 *Red Meat and Cancer Risk*

198 24. This was another issue that had been identified by a Member. It was
199 noted that the FSA's Scientific Advisory Committee on Nutrition (SACN) is
200 nearing completion of a draft report on iron, which addresses beneficial and
201 adverse effects of increasing iron intakes. Members considered it important
202 for SACN to consider the form of iron in red meat, since any carcinogenic
203 mechanism of action of haem iron is likely to be different to that of inorganic

204 iron. It was also noted that the recent World Cancer Research Fund report¹
205 on diet and cancer (2007) provided guidance based on a good review of the
206 evidence.

207 *Hair Dyes and Bladder Cancer*

208 25. A Member had suggested this item for horizon scanning. The
209 Secretariat explained that this was being dealt with by EU's independent
210 Scientific Committee on Consumer Products (SCCP). Members did not
211 consider there to be cause to investigate this further.

212 *Environmental Tobacco Smoke (ETS) Exposure in Childhood and Cancer* 213 *Risk*

214 26. A Member had suggested that the COC might examine cancer risk
215 following ETS exposure in childhood. A recent publication by the United
216 States' Surgeon General (USDHHS, 2007) was provided for information.
217 Members considered that, whilst this report examines the evidence for
218 childhood exposure to ETS and childhood cancer, it does not examine
219 childhood exposure and cancer in adulthood. Nevertheless, there was some
220 literature on this subject and members considered that this should be
221 reviewed.

222 *Chemo-protective Agents*

223 27. A Member asked whether the Committee should investigate
224 chemicals that reduce cancer risk. This was considered to be an immense
225 task that is beyond the terms of reference of the Committee which state that
226 the role of the Committee is to assess and advise on the carcinogenic risk
227 posed by specified types of chemical. Members questioned whether it should
228 be within the Committee's terms of reference to provide science based advice
229 on such agents.

230 *Overall Prioritisation*

Topic	Rank
Possible Carcinogenic Hazard from Dietary IGF-1	low
RNA Related Effects as Mechanism of Carcinogenicity	high / medium
Carcinogenic Risk Posed by Carbon Nanotubes	medium
Endogenous DNA Adducts (await COM view)	medium / high
Cupric Gluconate	not a priority
Red Meat and Cancer Risk	not a priority
Hair Dyes and Bladder Cancer	not a priority
ETS Exposure in Childhood and Cancer Risk	medium
Chemo-protective Agents	not a priority

¹ <http://www.dietandcancerreport.org/>

231 **ITEM 6.1: Chemical mixtures: the potential for chemical interactions in**
232 **carcinogenesis - CC/08/19**

233 28. The Committee considered a discussion paper on the ongoing review
234 of chemical mixtures which aims to explore the potential for chemicals to
235 interact in the carcinogenic process. Previously, the Committee had agreed
236 that a suitable strategy for the review would be to consider the multi-stage
237 nature of the carcinogenic process and to identify publications that attempt to
238 address how chemicals may interact at different points in this process.

239 29. Most papers retrieved in the review investigated polyaromatic
240 hydrocarbons (PAHs), including complex mixtures. *In vitro* and *in vivo*
241 approaches were used to assess potential synergistic responses and
242 assessed, variously, DNA adducts, tumour formation using initiation promotion
243 models and effects on the CYP family of enzymes, 1A1 and 1B1.
244 Heterocyclic amines (HCAs) were also identified as having potential
245 interactions. A number of studies suggested that HCAs may act
246 synergistically to promote tumours through a hypothesised CYP induction
247 mechanism. Members were asked to comment on the studies identified in the
248 review, the relevance of the studies to human exposure scenarios and the
249 implications for carcinogenicity testing.

250 30. Members noted that PAHs are known inducers of xenobiotic
251 metabolism and that this would be dependent on dose route, tissue, etc,
252 which would confound interpretation of studies of mixtures. A member
253 explained that, in one of his studies, CYP induction was observed at the
254 lowest biologically active dose. PAHs have been studied for many years and
255 results obtained *in vitro* and *in vivo* are often contradictory. It was considered
256 questionable whether CYP 1A1 activity was driving carcinogenicity *in vivo*,
257 since effects were still seen in aryl hydrocarbon receptor knockout mice.
258 Analysis of *in vivo* studies is difficult because pathways of metabolism,
259 activation and detoxification are inextricably linked. Members also questioned
260 the relevance of the SENCAR mouse model, which they considered to be
261 almost an *in vivo* genotoxicity assay.

262 31. The protocols of studies examining interactions between the HCAs
263 were very complex. It was noted that the pathology was poorly reported and
264 the method by which the data had been analysed was questionable. In the
265 study examining intestinal tumours, it was noted that the high incidence of
266 these tumours (45%) would make it difficult to detect an increase in incidence.
267 This high incidence might indicate cross contamination of the control group.
268 The Committee did not agree with the conclusion that there was evidence of
269 synergy, commenting that the conclusion relies on highly variable data at
270 higher doses. In addition to the high variability and high background, no dose
271 response data were provided. No null hypothesis was given and, therefore,
272 no statistical basis for acceptance and rejection of hypotheses; indeed it was
273 considered unlikely that the study would be able to distinguish between
274 hypotheses. Since few of the studies fulfilled the Borgert criteria (See
275 CC/08/19 Annex 1), the Committee decided that it was not possible to
276 comment.

277 32. An error (possibly typographical) was noted in table II of Ito *et al.*
278 (1991, Carcinogenesis 12: 767-772). The Secretariat suggested that the
279 32.02 mm²/cm² observed area of GST-P positive foci for the combined

280 treatment group receiving one fifth of the carcinogenic dose should read 2.02
281 mm²/cm². The Committee agreed and considered that this would impact on
282 the conclusion since it made the effect simply additive.

283 33. Members asserted that the terminology used in the paper could be
284 confusing since 'chemical interaction' could be taken to mean a physical
285 interaction between two chemicals, when what is actually meant is an
286 interaction between the biological responses resulting from exposure to the
287 individual chemicals. It was noted that there can be apparent synergy at
288 doses close to the threshold but that this would not necessarily be apparent at
289 higher doses above the threshold. It was considered possible that these
290 agents could increase the level of endogenously derived DNA adducts,
291 although it was noted that there were breakthrough mutations at higher doses.

292 34. Members considered that the postulated mechanism of interaction of
293 complex environmental mixtures and PAHs was succinctly discussed
294 CC/08/19. It was noted that the majority of interactions described involved
295 toxicokinetic alterations and it was difficult to put these into context with
296 interactions downstream in the carcinogenic process.

297 35. Members did not find the studies on HCAs convincing. It was noted
298 that the partial hepatectomy protocol will fix mutations occurring during the
299 period of regrowth and, since there was no clear effect even in this sensitive
300 system, the relevance to human health was considered questionable. It
301 should be acknowledged that these are mechanistic studies not
302 carcinogenicity studies.

303 36. With regard to recommendations for future research, Members
304 suggested that less complex protocols might lead to more informative studies.
305 It also should be considered likely that non-carcinogenic chemicals, such as
306 anti-apoptotic chemicals or chemicals interfering with cell cycle regulation,
307 might reasonably be expected to synergise with classical carcinogens.
308 Members commented that it might be too early to give advice on the risk
309 assessment and testing of mixtures of chemicals for carcinogenic effects.

310 **ITEM 6.2: Chemical mixtures: Mechanisms contributing to the**
311 **synergistic effects of asbestos and tobacco in human lung cancers -**
312 **CC/08/20**

313 37. Professor Phillips declared a personal specific interest as he had
314 been engaged as an expert witness in a court case on asbestos.

315 38. During the discussion of the interaction between alcohol and smoking
316 at the last meeting, Members suggested a number of other known interactions
317 which might be discussed. A paper was drafted to discuss synergistic
318 interaction between asbestos and tobacco smoking in causing lung cancer
319 and the mechanisms that might underpin this synergism. Members were
320 asked for views on whether the interaction was additive, multiplicative, etc.
321 and hypothesised mechanisms for the interaction.

322 39. Members considered that, whilst the paper was helpful, it did not
323 discuss the interaction models in sufficient depth to consider whether the
324 interaction was statistically significant. For example, is a multiplicative model
325 an interaction or a combination of two chemicals which exhibit a log-linear

326 dose response? The definition of additivity in an experiment was considered
327 to depend upon which model fits the individual chemicals. For asbestos, the
328 epidemiological data on different types of asbestos may fit different dose
329 response models. It was also noted that exposure misclassification might
330 lead to substantial uncertainty in epidemiological studies; this distortion in risk
331 estimates means that some studies give results consistent with additive risks
332 and others with multiplicative risks: systematic reviews suggest that the
333 combined risk is somewhere between the two models. It was also commented
334 that there were no specific discussions in some of the papers on the type of
335 asbestos fibres responsible for the induction of mesothelioma, with chrysotile
336 and amosite fibres thought to be responsible for 15% and 40% of induced
337 tumours respectively.

338 40. Members discussed the relevance of the latency period for tobacco
339 related lung cancer and asbestos related mesothelioma. It was noted that,
340 whilst mesothelioma risk stays constant over time following cessation of
341 exposure, lung cancer risk reduces when smoking ceases. This probably
342 reflects the fact that tobacco smoke is both an initiator and promoter of
343 cancer.

344 41. It was considered that, without knowing the individual mechanisms, it
345 is hard to interpret the short term studies; although it is possible to suggest
346 plausible hypotheses. It was noted that epigenetic mechanisms may also play
347 a part, or that asbestos exposure might increase uptake of carcinogens from
348 tobacco smoke. It was suggested that examination of the p53 mutational
349 spectra might offer some insights, as this is well defined for mutations arising
350 as a result of exposure to tobacco smoke. It might also be interesting to
351 examine the anatomical location of lung tumours, for example at bifurcations
352 of the airway, and the correlation of fibre deposition and tumour formation,
353 which might help elucidate a mechanical mechanism.

354 42. In conclusion, Members agreed that, although there was an indication
355 of a synergistic effect, there was insufficient evidence to estimate the strength
356 of synergy between the risks of lung cancer from asbestos and cigarette
357 smoking.

358 **ITEM 7: Preliminary report by SCHER, SCCP and SCENIHR on 'Risk**
359 **assessment methodologies and approaches for mutagenic and**
360 **carcinogenic substances' - CC/08/21**

361 43. The Committee was presented with a preliminary report by the EU
362 Scientific Committee on Consumer Products (SCCP), the Scientific
363 Committee on Health and Environmental Risks (SCHER) and the Scientific
364 Committee on Emerging and Newly-Identified Health Risks (SCENIHR); which
365 was under consultation until 2nd December 2008. Members were asked to
366 provide feedback on the areas covered by the COC terms of reference.

367 44. Members were complementary about the report, considering it to be
368 well considered and up-to-date. Concern was expressed about the discussion
369 of the T25 technique. Several organisations no longer support this
370 methodology due to its reliance on the lowest tested dose and lack of
371 consideration of dose response which makes the methodology inherently
372 more variable than the Benchmark Dose Modelling (BMD) approach.

373 Additionally the T25 method does not incorporate uncertainty in the analysis
374 of the data. Members were concerned that the document suggests that the
375 T25 and BMDL₁₀ are equivalent and implies that the T25 method should be
376 applied first. The recent presentation by International Life Sciences Institute
377 (ILSI) at the European Societies of Toxicology Congress (Eurotox) was
378 highlighted, where evidence was presented that suggested that the BMDL₁₀
379 was considerably superior to the T25 and where it was not possible to
380 determine a BMDL₁₀, it would not be possible to derive an informative T25 .

381 45. The derivation of the Margin of Exposure (MoE) uncertainty factor of
382 10,000 was also criticised. This retrospective justification for the magnitude of
383 the factor had never been adopted by the European Food Safety Authority
384 (EFSA). It was noted that this section cites “WHO 1987” and “WHO 1994”.
385 These are probably the Environmental Health Criteria (EHC) documents EHC
386 70 and EHC 170 which discuss derivations of uncertainty factors in general
387 but not the derivation of the factor of 10,000.

388 46. The International Programme on Chemical Safety (IPCS) mode of
389 action (MoA) framework was not mentioned in the report. This is a serious
390 omission since it is critical to understand whether there is likely to be a
391 genotoxic MoA underlying the carcinogenicity.

392 47. It was noted that the text does not reflect the more refined framework
393 for application of the Thresholds of Toxicological Concern (TTC) by Kroes.
394 This methodology should not be used indiscriminately and consideration
395 should be given to whether the chemicals under consideration are adequately
396 represented by the database used to develop the TTC approach. The
397 Chairman of the Committee on Mutagenicity (COM) indicated that there could
398 be some comments on the genotoxicity section of the reports, but noted that
399 the deadline for submission of comments was before the next COM meeting.
400 Members considered it reassuring that the report suggests basing judgements
401 on genotoxicity testing rather than other *in vitro* surrogates for carcinogenicity.

402 48. The Chairman asked for Members to pass any further comments to
403 the Secretariat which would compile a response to the consultation from the
404 Committee.

405 **ITEM 8: Is age an independent risk factor for chemically induced acute**
406 **myelogenous leukemia in children? - CC/08/18**

407 49. A recent review by Pyatt et al (2007; J Toxicol Env Health B,10(5)
408 379-400) tested the assumption that children are inherently up to 10-fold more
409 sensitive than adults to genotoxic carcinogens, using data on the
410 development of secondary or therapy-related acute myelogenous leukemia (t-
411 AML) in children who had received treatment with high dose chemotherapy
412 and/or radiation. This disease is well established as a potential long-term
413 consequence of exposure to such treatment. In their review, Pyatt et al
414 (2007) investigated the effect of age at treatment on a child's susceptibility to
415 developing therapy related AML. Members' views on the paper were sought
416 and they were asked whether the evidence might be used to address the
417 hypothesis that a sensitive population (children) might exist to benzene-
418 induced AML.

419 50. Members noted that there is still a paucity of information, which has
420 led the review authors to draw cautious conclusions. It was considered that
421 this evidence does not give cause to think that children are more susceptible
422 than adults, although the evidence is not strong enough to rule out such an
423 effect.

424 51. Members noted that the dose of chemotherapy is often scaled by
425 body surface area, using an algorithm incorporating height and weight,
426 whereas benzene inhalational exposure would be scaled relative to metabolic
427 rate (oxygen demand), on the basis of an exponent of the body weight. It was
428 acknowledged that, where susceptibility of the subpopulation is the result of
429 increased exposure, this would normally be incorporated into the risk
430 assessment by separate assessment of the exposure of the subpopulation,
431 with emphasis on children's specific exposure assessment.

432 **ITEM 9: Any Other Business**

433 52. The Chairman explained that he and Professor Boobis would be
434 attending a special meeting of the FSA's Scientific Advisory Committee on
435 Nutrition (SACN) to discuss a meta analysis of epidemiology studies
436 examining the relationship between folate intake and cancer. Since the SACN
437 meeting will be before the next COC meeting, it will not be possible to discuss
438 this at a full Committee meeting, although there may be an opportunity to
439 consult Members by e-mail

440 53. The Chairman thanked those retiring from the Committee and asked
441 Members to encourage suitable colleagues to apply for the vacant posts.

442 **ITEM 10: DATE OF NEXT MEETING**

443 54. 2nd April 2008.