

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

Minutes of the meeting held at 10.30am on Thursday 23rd July 2009 at
Department of Health, Room LG20/21, 133-155 Wellington House, Waterloo
Road, London SE1 8UG.

Present

Chairman: Professor D Phillips

Members: Dr C Allen
Professor A Boobis
Dr P Carthew
Professor P Farmer
Dr P Greaves
Dr D Lovell
Dr B Miller
Dr C Powell
Professor P Vineis

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

FSA Secretariat: Dr D Benford (Scientific Secretary)

In Attendance: Dr L Hetherington (HPA)
Mr K Mistry (DH)
Professor P Aggett (SACN Chair, item 4)
Professor T Key (SACN Member, item 4 & 6)
Mrs C Mulholland (FSA, item 4)
Ms M Singh (FSA, item 4)
Dr A Tedstone (FSA, item 4)
Dr S Reddy (DH, item 4)
Dr K Burnett (DH Tox Unit, item 5)
Mr D Renshaw (FSA, item 6)
Dr D Parker (FSA, items 5-6)
Dr K O'Leary (DH Tox Unit, item 7)
Dr P Edwards (HPA, UK National OECD
Coordinator, item 7)

Assessors: Dr D Gray (HSE)
Dr H Stemplewski (MHRA)

Observers: None

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ITEM 1: Apologies for Absence & Announcements

1. Apologies were received from four Members: Mrs R Glazebrook, Professor D Harrison, Dr N Wallis and Dr L Wright; and from Mr Paul Holley (Assessor, DH) and Mr Huw Brunt (Assessor, National Public Health Service for Wales)

Announcements

2. None.

ITEM 2: Minutes of meeting held on 2nd April 2009 (CC/MIN/09/1)

3. Members requested that the wording of the reference to the IARC publication on complex mixtures and cancer risk in paragraph 17 should be checked for consistency with the original document¹.

ITEM 3: Matters arising not covered by later agenda items

4. None.

ITEM 4: Draft SACN Report on Iron and Health (CC/09/5)

5. The FSA's Scientific Advisory Committee on Nutrition (SACN) had asked for the COC's advice and opinion on the evidence for the relationship between red and processed meat consumption and colorectal cancer risk. The Committee had been provided with the draft SACN report on Iron and Health, which summarises the available epidemiological and mechanistic evidence.

6. Professor P Vineis declared a non-personal specific interest because he is a co-author of some of the papers on investigations in the European Prospective Incidence of Cancer (EPIC) cohort. Dr Carthew declared a non-personal specific interest because his employer manufactures products containing processed meat. These interests were noted and it was considered appropriate for both members to fully participate in the discussion and formulating the Committee's conclusions. Professor Key, a member of SACN, informed the Committee that he had authored some of the epidemiological studies under consideration and that he is a member of the Vegetarian Society.

7. Professor P Aggett, the Chairman of SACN Working Group on Iron, provided a brief background of the draft report and informed the Committee that there were a number of uncertainties in the data. With reference to cancer, the SACN report concludes that red and processed meat is "*probably*" associated with colorectal cancer (CRC). He noted that the SACN advice was more moderate than that of the World Cancer Research Fund (WCRF) report

¹ Vainio H, Sorsa A, McMichael AJ. Complex mixtures and cancer risk. IARC scientific publication no. 104, 1990, Lyon.

on diet and cancer², which concluded that red and processed meat is a “convincing” cause of CRC.

8. Professor T Key, a member of SACN with epidemiological expertise, explained that although there were high quality studies, many of the early studies were small and low powered. He noted that measurement uncertainty in estimating dietary meat consumption tends to reduce the relative risk. He explained that a major problem with the studies in this area is confounding since a number of lifestyle factors that are associated with meat intake (such as obesity, alcohol consumption, smoking, lack of exercise) are also risk factors for CRC. Whilst some studies correct for these confounders, residual confounding is likely.

9. Professor Key highlighted the four largest prospective studies, which each draw on over 1000 cases. The study by Wei *et al.* (2002)³ showed increasing but non statistically significant CRC risk with increased intake of red meat. The study by Chao *et al.* (2005)⁴ also showed a non-significant increased CRC risk in the highest compared to the lowest exposure quintile, although the trend test reached significance. In this study there was a substantial reduction in relative risk following adjustment for possible confounding factors. The EPIC study (Norat *et al.*, 2005)⁵, did not show a significant association after full adjustment for confounding. The largest study, by Cross *et al.*(2007)⁶, which included a cohort of 0.5m people, with 5100 cases, reported a significantly increased risk of CRC when upper and lower quintiles of consumers were compared (risk ratio, 1.24; 95% CI, 1.12-1.36).

10. With regard to the studies which had examined the relationship between processed meat and CRC risk, Professor Key noted that the definition of processed meat is not consistent in all the studies. All four of the main studies reported a statistically significant positive trend for consumption of processed meat and CRC, however confounding may be more of a problem in studies of processed meat. Dr Tedstone, from the FSA SACN Secretariat, explained that the typical UK diet contains about 80 g of meat per day and that processed meat contributes half of the intake. However, it is difficult to compare the quantities consumed in various studies since the assumptions regarding processed meat content of recipes vary.

11. Professor Key also tabled 2 papers reporting findings from his own research^{7,8} which indicated that CRC cancer incidence is not reduced

² World Cancer Research Fund. Food, Nutrition, Physical Activity and the Prevention of Cancer: a global perspective. 2007. <http://www.dietandcancerreport.org/>

³ Wei EK, Giovannucci E, Wu K, Rosner B, Fuchs CS, Willett WC, Colditz GA. Comparison of risk factors for colon and rectal cancer. *Int J Cancer* 2004; 108(3):433-442.

⁴ Chao A, Thun MJ, Connell CJ, McCullough ML, Jacobs EJ, Flanders WD, Rodriguez C, Sinha R, Calle EE. Meat consumption and risk of colorectal cancer. *JAMA* 2005; 293(2):172-182.

⁵ Norat T, *et al.* Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. *J Natl Cancer Inst.* 2005; 97(12):906-16

⁶ Cross AJ, Leitzmann MF, Gail MH, Hollenbeck AR, Schatzkin A, Sinha R. A prospective study of red and processed meat intake in relation to cancer risk. *PLoS Med* 2007;4(12):e325.

⁷ Key TJ, Appleby PN, Spencer EA, Travis RC, Allen NE, Thorogood M, Mann JI. Cancer incidence in British vegetarians. *Br J Cancer.* 2009;101(1):192-7.

12. Members agreed that although the majority of the studies indicate red and processed meat intake is associated with increased CRC risk, the evidence is not unequivocal. It was noted that meat consumption varies with socioeconomic status (SES) and that eating meat is associated with many other lifestyle factors; therefore, all studies will be subject to considerable confounding which is unlikely to be completely removed during epidemiological analysis. However, the impact of confounding should not be overstated because residual confounding is unlikely to entirely explain the observed increased risk reported in most studies. It was agreed that any recommendations should take account of the biological and epidemiological limitations of the evidence base.

13. It was observed that genetic predisposition is unlikely to be a potential confounder, except in particular circumstances. However, it is possible that dietary preferences might be influenced by *perceived* familial susceptibility to disease.

14. Evidence of non linear trends was discussed. Professor Key explained that trend analysis is more powerful than simply comparing exposure quintiles and that the data are insufficient to demonstrate a quadratic trend.

15. Members considered the various potential biological mechanisms for the association between red and processed meat and CRC risk. It was noted that the hypothesis that the link between meat and CRC may be due to heterocyclic amines (HCA) produced during the cooking of meat had weakened, as recent studies had failed to show an association between meat 'done-ness' and cancer. The Margin of Exposure (MOE) between carcinogenic dose in experimental studies and human exposure is very large, which does not support HCAs as a major causative factor in human cancer aetiology. Members noted that there was not strong evidence linking CRC risk with N-nitroso compounds, which are found in processed meats, and it was noted that endogenous formation can exceed exogenous exposure. Members also considered oxidative stress associated with the iron contained in meat, although it was noted that the majority of dietary iron comes from vegetables, supplements and fortified foods. Overall, although each mechanism was considered plausible, none was supported by robust evidence.

16. The Committee discussed the wording of the SACN conclusion: *“overall the available evidence suggests that red and processed meat is probably associated with increased colorectal cancer risk. However since the evidence is based on prospective observational studies, the effects of confounding by other factors associated with increased colorectal cancer risk*

⁸ Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Cancer incidence in vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr.* 2009; 89(5):1620S-1626S.

cannot be excluded". Members were concerned with use of the word *'however'* in relation to prospective observational studies as this type of study can be one of the most informative. The use of the words *'probably associated'* was also questioned as it would be more helpful to state either that the data were limited but showed an effect, or that the data were substantial but equivocal.

17. It was noted that WCRF considered that the evidence is "*convincing*", although WCRF remit was slightly different to that of the SACN review. Members were conscious that both SACN and WCRF had reviewed the critical studies in this area, whereas the COC view was being sought based on the evidence presented in the SACN consultation document. Thus, the Committee was not provided with sufficient evidence to advise on whether the choice of "*probable*" or "*convincing*" was more appropriate.

18. Members supported the conclusion that there is an association but it is not known whether the relationship is causal. It was suggested that the conclusion should be re-worded to make this clearer and that this should also feature prominently in risk communication. Members also concluded that, even with the residual uncertainties, any risk appeared to be small.

19. The SACN Chairman and Secretariat thanked the COC for providing valuable feedback.

ITEM 5: Chemical Mixtures

ITEM 5.1: Draft Statements on the Assessment of the Carcinogenicity of Chemical Mixtures (CC/09/06)

20. At the previous meeting, Members were presented with a first draft statement. Although there was limited time to discuss the statement in depth, Members were keen for the statement to be restructured into two statements. This had been done and it was explained that the first statement covers general principles and theoretical exploration of the effects of combinations of carcinogenic chemicals such as the PAHs. The second statement focuses on the examples of potential interactions taken from epidemiological studies which were discussed by the Committee (alcohol and tobacco, and tobacco and asbestos). The Secretariat had received a few additional comments and suggestions, which have been incorporated into the second draft.

21. Members noted that this is a challenging topic. It was considered that there should be detailed discussion of the Mode of Action (MoA) concept, which has been developed to allow the evaluation of more than one chemical acting through the same mechanism. There needed to be a clear rationale for combining chemicals based on MoA e.g. several chemicals acting on the same receptor. It was asserted that genotoxicity should not be considered to be a MoA, but as a potential key event in disease aetiology.

22. Consideration of mixtures in the absence of a common MoA is highly uncertain because there is not enough experimental data on how chemicals with diverse MoAs would combine. Proof of principle experiments in model systems could be conducted to examine a combination of chemicals of diverse MoAs where interaction might reasonably be expected; such as

23. It was noted that there was some inconsistency in the use of the term 'interaction' (page 3 of the first statement referred to a deviation from the expected, whilst page 10 of the second statement talked about a joint effect). This should be clarified. In addition, it was agreed that a paragraph on statistical dependence would be helpful and two members offered to draft a paragraph on this.

24. There was no mention of good principles of experimental design, several of which have been developed for mixtures studies. It was noted that these study designs are generally suitable for short duration studies and would be unfeasibly complex for long term carcinogenicity studies. The ethics of using a considerable number of animals in such a study would also need consideration. The Committee did not consider it wise to recommend conducting a large number of long term carcinogenicity studies where there is robust examination of the interactions between components. It would be more realistic to conduct mechanistic studies that may suggest the likely direction and magnitude of effect of a combination of chemicals.

25. It was reiterated that thorough understanding of the dose response for the individual components of the mixture is necessary in order to determine when there is deviation from additivity. Regarding the strength of the conclusion on the contribution of otherwise non-carcinogenic compounds (such as apoptosis inhibitors), it was considered wise to refer to them having the 'potential to interact synergistically', rather than being 'reasonably expected to interact'.

26. In the second draft statement, providing examples of potential interactions, Members asked for the phrase "limited but convincing" to be clarified. It was noted that paragraph 8, line 11 talks about a null hypothesis, which requires further explanation. In the same paragraph, line 17 implies some fundamental difference between asbestos and tobacco smoke following removal from the source of exposure. However, whilst smoking cessation will allow residual smoke residue to be cleared from the lungs, asbestos fibres would be retained in the lung after removal from the source of exposure. Hence, the sustained exposure to the causative agent long after removal from the source of exposure is a major difference between these two carcinogenic substances.

27. Members were asked to carefully scrutinise the statements since the referencing of some aspects of the paper could be improved. They were also asked to consider whether the definitions are appropriate, and whether effect and response addition should be considered to be synonymous. The Secretariat will redraft the statements for further discussion at the next meeting.

ITEM 5.2: WHO/IPCS Harmonization Project: Framework Document for Review (CC/09/07)

28. The World Health Organisation (WHO) International Programme on Chemical Safety (IPCS) has issued a draft of the document 'Risk Assessment

Comments were invited from groups and individuals with an interest in the area. The document was provided together with two worked examples using the suggested tiered system: polybrominated diphenyl ethers and carbamates. Members were invited to provide comments which would be passed back to the WHO.

29. Professor Boobis declared that he had been involved in the Committee that authored the document. This was noted but not considered to preclude full participation in the discussion. He noted that he had gained permission from the Interdepartmental Group on Health Risks from Chemicals (IGHRC) to share its work on mixtures with the WHO Committee

30. It was noted that the methodology described was only applicable to chemicals acting by a common mode of action. Members considered it useful that the document developed the two parallel tiered approaches for exposure and hazard assessment. This is a novel approach and the strategy which had recently been used by the European Food Safety Authority (EFSA) panel on plant protection products and their residues (PPR), in an opinion on triazoles (yet to be published). EFSA had collapsed the approach into three tiers.

31. It was commented that discussion and development of hazard index / quotient would have been helpful, although it was noted that discussion of hazard indices are included in other IPCS documents which was why it had not been repeated here. It was noted that this approach was intended to aid the assessment of a low level of exposure to a mixture, not high level / occupational exposure.

32. The worked examples were considered to greatly enhance the document. It was noted that the generic diagram in the second example needed to be modified to relate to the specific scenario, as had been done for the first example. It was considered important to emphasise that, whilst the worked examples moved up through the tiers, in reality, it is anticipated that risk assessors would stop at the tier providing a satisfactory or reassuring risk assessment.

33. It was observed that tier 0 constituted a particularly crude and conservative risk assessment, with the progression up through the tiers generally reflecting increasingly refined risk assessments, moving away from conservative assumptions to realistic parameters. Looking specifically at the polybrominated diphenyl ethers (PBDE) worked example, biological persistence was not considered, with congeners being selected on the basis of usage. Members considered the persistence to be an important factor in the risk assessment, but noted that tier 0 was intended to be very crude, including the broadest membership of the common mechanism group. Also, it was noted that REACH still identifies chemicals based on production volumes.

34. The Secretariat undertook to pass the Committee's comments back to the IPCS.

⁹IPCS Risk Assessment of the combined exposures to multiple chemicals:
http://www.who.int/ipcs/methods/harmonization/areas/combined_exposure/en/index.html

ITEM 6: Possible carcinogenic hazard to consumers from insulin-like growth factor-1 (IGF-1) in the diet (CC/09/08)

35. It was explained that a member of the public had contacted the FSA and the Veterinary Medicines Directorate (VMD) with concerns about the import of dairy produce from countries that allow the use of bovine somatotropin (BST) in cows. The use of BST was said to increase the amount of insulin-like growth factor-1 (IGF-I) in milk, and there was concern that increased dietary exposure to IGF-1 might increase the risk to consumers of developing cancer. The concern had been prompted by issues raised in the book "Your Life In Your Hands" by Professor Jane Plant. In the book, the author suggested that consumption of IGF-1 in dairy produce could lead to an increased risk of developing certain cancers, particularly of the breast and prostate.

36. Members were informed that, in July 2008, the Veterinary Products Committee had reaffirmed its opinion from 1999 that it could not exclude the possibility that dietary IGF-I might cause cell proliferation of the gut mucosa with the potential to increase the prevalence of carcinoma of the large bowel.

37. The Secretariat had raised the issue of the possible carcinogenic hazard from dietary IGF-1 during the horizon scanning discussion in November 2008. The COC observed that there are broader concerns relating to dairy products and cancer risk than just exposure to IGF-1. It was suggested that the Secretariat should examine the evidence presented in Professor Plant's book and that, if adequate data are presented, these should be brought back to the Committee for review. Thus, the Committee was presented with a summary of the scientific evidence base cited in the book; along with draft conclusions for Members to consider. Members were asked whether the Committee should conduct its own review of the potential for dietary IGF-1 to increase the risk of cancer in consumers.

38. Dr Lovell declared a non personal specific interest, in that his university had previously been paid by the Dove Clinic for Integrated Medicine, for which Professor Plant is a member of the Advisory Board. The advice was on statistical analysis not relating to IGF-1. This was noted but not considered to preclude full participation in the discussion.

39. Professor Boobis declared that he had been a member of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) during the assessment of BST. This was also noted but not considered to preclude full participation in the discussion.

40. It was noted that there were at least two large studies that did not appear to be mentioned in the book. Professor Key was invited to speak about a recent publication from the EPIC cohort, which showed a positive association between intake of dairy food and serum IGF-1 levels. He also described a study in which boys received protein either in the form of milk or meat. IGF-1 levels were only increased in those receiving milk. He considered that it is probable that increased IGF-1 levels are associated with the consumption of dairy products, although there is insufficient evidence for a potential mechanism. It was also noted that there was some evidence that IGF-1 levels appear to be linked to milk yield, irrespective of BST treatment.

41. Members observed that IGF-1 is used therapeutically to treat growth disorders; hence, there should be a package of preclinical and possibly clinical data to support its safety.

42. It was considered highly unlikely that dietary IFG-1 could elicit an effect in the gastrointestinal tract. The weight of evidence is that preformed IFG-1 will not be absorbed intact from the gut to any great extent. It is also unlikely that the cells of the intestinal epithelium would respond to luminal growth factors. The book mentions that the truncated form of IGF-1 may be of increased potency and may also be present in milk. It was considered appropriate to ensure this information is representative of the typical concentrations in milk.

43. The draft conclusions were examined:

- 1) *The book presented evidence on the role of IGF-I in cell proliferation and cancer in support of a claim that risks of certain cancers, particularly breast and prostate cancers, are increased by consumption of dairy products and that the increased risk is a result of the presence of IGF-I in milk. The evidence presented was incomplete, and of inconsistent quality, so any conclusions drawn from the book must be regarded as provisional and would need to be confirmed following a fuller systematic search of the scientific literature before they could be acted upon.*

This draft conclusion was agreed since the book clearly does not present a balanced systematic review of the available literature.

- 2) *The book identified that IGF-I has a role to play in the normal growth and development of tissues, and that locally high levels of IGF-I or increased sensitivity to IGF-I can also cause cancer cells to multiply. Thus IGF-I is one of the many substances that have been shown to play a role determining the growth and development of cancers.*

It was considered that this draft conclusion should emphasise that evidence that IGF can stimulate cancer cell growth has been generated in vitro. It was also considered that implying that IFG-1 has “been shown to play a role determining the growth and development of cancers” may be an over interpretation of the evidence, so this sentence should be removed from the conclusions.

- 3) *The book did not provide convincing evidence to justify the claim that the IGF-I in milk and dairy products (or in any other food) could cause consumers to have increased risks of developing certain cancers.*

Members noted that no data had been presented on IGF-1 concentrations in foods other than milk and that without such information it was not possible to determine whether there is an epidemiological association between dietary IGF-1 intake and cancer.

- 4) *[duplicate deleted]*

- 5) *Information was provided on the amount of IGF-I in milk, but nothing was presented on the amounts of IGF-I in other foods.*

Members were content with the fifth draft conclusion

- 6) *There is a potential for dietary IGF-I to come in contact with the cells lining the gastrointestinal tract. However, no information was presented on the concentrations of IGF-I that these cells could be in contact with.*

Members were content with the sixth draft conclusion

- 7) *No information was presented on the amount of breakdown of IGF-I that might occur in the gut lumen, although there was some evidence that casein and some other dietary proteins might give some protection from breakdown and there was evidence that partial breakdown to N-terminally truncated forms could increase the potency of IGF-I*

The seventh draft conclusion mentioned protection of IGF-1 from breakdown, conferred by casein. It should be emphasised that this evidence was obtained *in vitro*.

- 8) *No information was presented on the amount of IGF-I from dietary sources that might be absorbed from the gut lumen into the bloodstream*

Members were content with the eighth draft conclusion.

- 9) *There was evidence (in the book?) that showed that IGF-I could cause mitosis and apoptosis to occur in vitro in some cell lines, including several derived from cancer cells. It was also claimed that IGF-I caused differentiation of cells, but the references that were cited presented no evidence from experiments in support of the claim.*

Members considered that the ninth draft conclusion was a repeat of the second and that the two should be merged. Professor Key observed that the reference to IGF-1 causing apoptosis appears to be incorrect. Members requested that this be checked with the statements made in the book.

- 10) *The book presented evidence that showed an association between blood levels of free IGF-I and risks of some cancers. However, it was not clear whether the cancers were caused by the high IGF-I or whether the high IGF-I was a consequence of the cancers.*

With regard to the tenth draft conclusion, it was considered important to clarify whether the book claimed that the evidence demonstrated a causal link. The second sentence should be deleted because reverse causation can be excluded.

44. The Committee considered that a systematic review on the risk of cancer from dietary IGF-1 would be worthwhile and agreed with the Secretariat's proposed strategy. As regards additional lines of enquiry, the Committee suggested obtaining the preclinical data package for therapeutic use from the US Food and Drug Administration (FDA); although Members were cautious as to the relevance of data on the effects of injection of a potent mitogenic peptide to the potential risks of exposure via the oral route. It would be helpful to know whether dietary IGF-1 contributes to circulating IGF-1 levels. It was also suggested that expressing the mitogenic potency of IGF-1 in relation to a benchmark, such as oestradiol, might give some idea of the biological plausibility of the purported increase in cell proliferation.

ITEM 7: OECD guidance document on chronic toxicity and carcinogenicity studies - Chapter 3.6: Investigations (including Histopathological Guidance) (CC/09/09)

45. The Organisation for Economic Cooperation and Development (OECD) is currently developing a Guidance Document to accompany the revised Test Guidelines for carcinogenicity studies and chronic toxicity studies. The UK agreed to draft chapter 3.6 on investigations including histopathological guidance which is to include advice on all investigations. Members were asked to comment on the second draft of the chapter, which had been revised to take into account Members' comments and to remove text available elsewhere in OECD guidance (GD35).

46. This was considered to be a useful and well referenced document. Concern was expressed at the use of the term 'negligent handling' in paragraph 36. This was intended to refer to incidents such as accidental mis-dosing in gavage studies; Members requested that a better form of words be used to reflect these incidents. The term 'balanced design' in paragraph 42 was also queried. It was suggested that this be defined in the text, by explaining that this refers to systematic ordering within the study (dosing, machines etc.) so as to limit the effect of unforeseen variables. Also, it may make the document seem somewhat out of date to refer to random number tables for randomisation, when this is now more likely computer generated. The term signalment was queried; it was explained that this refers to other information about the animal (sex, etc.).

47. It was considered important for the guidance document to address the issue of incidental background lesions (which may occur due to infections etc.). These may mask or modulate other toxic effects, so should not be edited out of the study report and any correction should be transparent. This guidance should be added to the initial pathology section and reiterated in the peer review section of the chapter.

48. Members noted that some health and safety comments were contained within the document, for example, regarding the use of picric acid. This should be extended to other chemicals used in pathology/histology, such as formalin and xylene. The UK OECD National Coordinator pointed out that a paragraph indicating safer alternatives to formalin and xylene was included in the document. It was acknowledged that the guidance was not intended to provide detailed operating procedures.

49. The UK OECD National Coordinator thanked the Committee for its helpful comments, which will be taken into account in the revision of the draft Chapter. The Guidance will be further discussed at the OECD.

ITEM 8: Information paper: SCCP Opinion on oxidative hair dyes and cancer: Opinion on intermediates and reaction products of oxidative hair dye ingredients formed during hair dyeing (CC/09/10)

50. This paper was presented for information and not discussed at the meeting

ITEM 9: Any Other Business

51. None.

ITEM 10: DATE OF NEXT MEETING

52. 19th November 2009 at Skipton House, Elephant and Castle, London SE1 6LH.