Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Minutes of the meeting held on Tuesday, 22nd June 2010 in Aviation House, London.

Present

Chairman: Professor D Coggon

Members: Mr D Bodey
          Professor A Boobis
          Dr R Dearman
          Professor D Harrison
          Professor B Houston
          Professor J Konje
          Professor B Lake
          Professor I Morris
          Dr N Plant
          Items 7 to 12
          Professor R Smith
          Dr J Thompson

FSA Secretariat: Dr D Benford (Scientific Secretary)
                Mrs J Shroff (Administrative Secretary)
                Dr D Gott
                Dr D Key
                Ms C Mulholland
                Dr D Parker
                Dr J Shavila
                Mr G Welsh

HPA Secretariat: Mr J Battershill Health Protection Agency
                 (HPA)
                 Dr L Hetherington HPA
                 Item 4

Assessors: Dr O Sepai HPA
           Dr C Pease Environment Agency
           Dr M Roberts Department of Environment,
           Food and Rural Affairs
Other officials in attendance:

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<td>FSA Press Office</td>
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Invited experts and contractors:

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<td>Dr S Ermler</td>
<td>University of London, School of Pharmacy</td>
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<td>St. George's University of London</td>
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External observers: None
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- **Announcements**

1. The Chairman, Professor Coggon welcomed the invited expert, Professor Omer Van den Bergh of the Research Group on Health Psychology, University of Leuven, and also Dr Ovnair Sepai, head of HPA General Toxicology and Biomonitoring Unit, who attended the meeting as an assessor.

2. The Chairman announced that Dr David Tuthill had resigned due to pressure of other commitments. Dr Tuthill had made an excellent contribution to the work of the Committee and he would be missed; this was to have been his last meeting, but he was unable to attend.

3. The Chairman confirmed that an advert for new members had been published, and circulated to Members on the 28th May. The Chairman encouraged Members to forward it on to any suitable experts.

4. The Chairman reminded those attending the meeting to declare any commercial or other interests that they might have in any of the agenda items.

- **Item 1: Apologies for absence**

5. Apologies for absence were received from Drs Tuthill, Hansell, Elcombe and Foster. Dr Hansell had submitted a written comment.

- **Item 2: Draft minutes of the meeting held on Tuesday, 4th May 2010 – TOX/MIN/2010/03**

6. The minutes of the 4th May 2010 meeting were agreed subject to the following amendments (in italics):

   - List of Members present at the meeting should include “Professor D Harrison”
   - Para 8, line 9: “agricultural land over the next few months.”
   - Para 31, line 1: “Norris et al. (J.A.M.A. 290, 1713-1720, 2003)”
   - Para 32, line 3: “Norris et al. (J.A.M.A. 290, 1713-1720, 2003) and Ziegler et al. (J.A.M.A. 290, 1721 – 1728, 2003).”
   - Para 40, line 3: “since they indicated that less methanol was produced from aspartame endogenously or ingested from dietary sources such as apples, than was obtained from aspartame.”
   - Para 41, line 3: “if the model was to work be useful”
Item 3: Matters arising

Landfill

7. Further minor amendments were still required to the draft statement before it could be finalised by Chairman's action.

NHANES

8. A further paper would be available for the next meeting. A member had provided for information a paper on type 2 Diabetes Mellitus that exploited data from the US National Health and Nutrition Examination Survey (NHANES) in a novel way.

Timing of introduction of gluten into the infant diet

9. This would be discussed by the SACN Subcommittee on Maternal and Child Nutrition on 8th September. The Chairman and Dr Dearman had been invited to attend to present the views of COT.

Chronic toxicity of methanol

10. A further paper would be available for the next meeting.

Pre-Election restrictions

11. The Chairman had raised Members' concerns regarding the pre-election restrictions on independent advisory committee business, asking that they be discussed at the next meeting of the General Advisory Committee on Science (GACS).

Item 4: Draft discussion paper on Idiopathic Environmental Intolerance (IEI) and behavioural conditioning – TOX/2010/14

12. No interests were declared.

13. In October 2009, COT considered a discussion paper that presented an overview of the evidence relating to possible toxicological mechanisms of idiopathic environmental intolerance (IEI). The COT had agreed that they also needed information on psychological aspects of IEI to assist them in their provision of advice. The discussion paper TOX/2010/14 provided information on the principles of behavioural conditioning, sensitisation and generalisation, and their potential relevance to the development of IEI.
14. Anonymised peer review comments on the paper were provided in Annex 1. These supported the conclusion, based on experimental and epidemiological studies and clinical observations, that IEI could in many cases arise through behavioural conditioning. Furthermore, once learning had taken place, toxicological mechanisms would not be required to explain the future re-occurrence of symptoms. The reviewers noted the geographical differences in the prevalence of reported symptoms of intolerance, for example in relation to mobile phone base stations.

15. Professor Omer Van den Bergh, from the Research Group on Health Psychology, University of Leuven gave a presentation entitled “Idiopathic Environmental Intolerance: A Laboratory Model”. He reported that IEI was similar to other functional syndromes (such as chronic fatigue syndrome, fibromyalgia, sick building syndrome and electrosensitivity), across which there was a large overlap of symptoms, with similar patient characteristics (e.g. high psychiatric co-morbidity) and similar response to the same therapies (e.g. cognitive behavioural therapy). The presentation discussed the conventional disease model and explored the way in which conditions such as IEI deviated from that model. He proposed a biopsychosocial model, in which symptoms are not a direct and immediate effect of physiological dysfunction, but are importantly influenced by psychological processes. Professor Van den Bergh explained that conditioning could occur, with the result that symptoms could subsequently be triggered in the absence of toxic exposures. Behavioural conditioning experiments were described in which volunteers were exposed to odours in carbon dioxide enriched air, the carbon dioxide causing hypercapnic hyperventilation. The hyperventilation symptoms could then be produced by exposure to the odour in the absence of elevated carbon dioxide. The nature of the odour, the effect of the experiment’s context (what the experimenters said about the nature of the odour and the volunteers’ expectations) and accompanying neutral or negative imagery had all been found to influence the conditioning process. The predisposing effect of personality was noted, hyperventilation being more marked and persistent in subjects with high negative affectivity. He noted the key role of negative affective cues. Professor Van den Berg also described the process of generalisation, by which responses to ‘foul’ odours generalised to other, not previously experienced odours. He noted that the threshold for report of symptoms by individuals with high negative affectivity was low, with a tendency to over-evaluate symptoms. He speculated on neuronal processes that could be involved in IEI, which might involve inhibitory effects on prefrontal processing of information.

16. Members thanked Professor Van den Bergh for his presentation and asked a number of questions.

17. It was asked whether an allergic response could trigger the development of a conditioned response. It was agreed this might be the case, and noted that in a study of patients with asthma, almost half the variation in respiratory symptoms was unrelated to lung function, some patients over–experiencing symptoms and others under–experiencing them.

18. It was asked whether subjects with low negative affectivity could be influenced by those with high negative affectivity or by other people’s experiences. It was explained that the personality of the subjects was a most important risk factor. This
might be determined by genetic differences or by differences in brain function. High negative affectivity was an important risk factor for psychological complaints, for stress-related illness and for stress-related behaviour producing symptoms such as hyperventilation. Where people had an acute hyperventilation response to triggering odours, they could learn to distinguish the odour and the symptoms and ‘unhook’ the link. However, this was much more difficult for people who experienced more chronic symptoms. Although there were no pertinent studies in patients with clinically diagnosed IEI, it appeared that in subjects with low negative affectivity, the reaction could be extinguished over time without intervention. However, in subjects with high negative affectivity this was more difficult since they were subject to reinforcing and avoidance behaviour. A case was then described in which a patient had been exposed to steam and dishwashing chemicals in an industrial kitchen, resulting in hyperventilation and panic attacks on subsequent exposure to steam alone. Pre-frontal lobe inhibitory control was possibly involved in the response. The symptoms involved a change in physiology in several regions of the brain, even when an exposure was only expected and had not actually occurred.

19. Members asked what other research was being conducted in the same area and whether the results were compatible. Professor Van den Bergh explained that his studies had been done on volunteers rather than patients, and that while no other groups were working in precisely the same area, comparable studies of brain function were being conducted for related illnesses such as chronic fatigue syndrome.

20. It was asked whether the responses were culturally conditioned. Professor Van den Bergh responded that patterns of symptoms were fairly consistent over time, but the names given to the syndrome had changed.

21. A member was asked to comment on immunological aspects of IEI. It was noted that when immunotoxicity had been considered as an inducing factor, it had been proposed that CD4 and CD8 lymphocytes could be involved. It had been reported that the numbers of CD8 cells were outside the normal range and this was considered at that time to be evidence of potential immunosuppression. However, it is now known that a different population of T cells (Treg cells) is involved in immunosuppression, and changes in CD8 lymphocytes are no longer considered to be indicative of immunosuppression. Data associating IEI with immune cell numbers were not strong, but there did seem to be an overlap with allergic disease (such as hay fever) in that there were a lot of allergic subjects among people with IEI. However, the observation related to self-reported symptoms rather than to positive skin-prick tests. It was possible that among people with IEI, some were mis-diagnosed and in fact had uncontrolled allergic disease, some had both allergy and IEI, and others had IEI alone.

22. Members were asked for any general comments on the paper. There was some discussion on whether it was appropriate to refer to these as psychosomatic conditions. Although there were some reservations about the term, the alternative of “medically unexplained” was felt to be unhelpful. It was noted that psychological factors contributed to the experience of symptoms and all illnesses, even where there was clear underlying disease such as cancer. However, some patients were very uncomfortable with the suggestion that their symptoms might arise through
psychological mechanisms. It was further remarked that in the context of IEI, “sensitisation” did not refer to an immunological process.

23. The comments of the peer reviewers were noted, and the Committee agreed that there was also relevant evidence from observational epidemiology. For example, electro-sensitivity was unusually prevalent in Sweden, while attribution of symptoms to low level exposure to organophosphates appeared to be more common in the UK than in other countries.

24. Members were asked whether, based on the information presented, a toxicological mechanism (either receptor-mediated or idiosyncratic) for IEI could be discounted? It was agreed that there was not enough evidence to discount a toxic mechanism in all cases.

25. Members agreed that there was plausible evidence for a substantial role of psychological mechanisms in IEI, which should be considered further by the appropriate specialism within the Department of Health (and devolved administrations), as this might point the way to the development of treatments. It was noted, however, that there were relatively few published data on patients.

26. It was agreed that the COT should publish a statement on IEI relating to toxicological mechanisms, but including reference to the evidence for psychological mechanisms. This would need to be worded carefully to ensure that it was scientifically robust, and that it did not give the misleading impression of dismissing a genuine, and sometimes severely disabling illness. It was suggested that in discussing possible toxicological mechanisms, the statement should highlight the unusual features of IEI which any unrecognised toxicological mechanism would need to explain (such as the occurrence of a similar response to a wide range of structurally diverse compounds).

27. The statement should also refer to the strong evidence for a substantial psychological component to IEI, but make clear that there were psychological aspects to all illnesses. It was noted that IEI sometimes responded to cognitive-behavioural therapy, which again supported a psychological component to the illness.

Item 5: Definition of an endocrine disrupter for regulatory purposes – TOX/2010/15

28. The classification of substances as endocrine disrupters has become important in a number of regulatory contexts. The Committee was asked to comment on a paper that proposed a definition, and method for determining whether a substance is an endocrine disrupter, which might be applied in the context of legislation relating to plant protection products, biocides and the Registration, Evaluation, Authorisation and Restriction of Chemical substances (REACH). The Committee’s views would be used by the Health and Safety Executive to feed into and inform European Union discussions. It was noted that the discussions and recommendations from the meeting could have implications with respect to environmental chemicals more widely.
29. Members noted that in European Union legislation, endocrine disruption, along with carcinogenicity, mutagenicity and teratogenicity, had been singled out as hazard triggers of special concern. The scientific basis for treating endocrine disruption differently from other toxic modes of action was debatable. Members considered that current evidence did not indicate special features that warranted a different approach. For example, there was strong evidence of monotonic dose/concentration-response relationships in vitro and in vivo, and non-monotonic effects seemed unlikely. Moreover, additivity at the estrogen receptor was in essence no different from that for other receptor-mediated effects. However, a Member drew attention to evidence from environmental studies that endocrine disrupters can adversely affect reproductive growth rates in populations of wild animals.

30. It was noted that paper TOX/2010/15 appeared to have been written with data-rich compounds such as plant protection products in mind. Where fewer data were available, as was likely to occur under REACH, chemicals might have to be assessed using predictive in vitro systems or read across from structurally related substances. For example, if there was evidence that a substance was more potent in vitro than estradiol, and kinetic data indicated that it was not cleared rapidly, then it should be unnecessary to undertake an animal study before classifying it as an endocrine disruptor.

31. Members discussed the proposed definition of an endocrine disrupter. It was suggested the definition might be considered to be too much of a “catch-all”, and that it should capture concepts of potential to alter function based on mode of action and dose. Incorporating “the potential to alter function(s)” would allow for use of results of predictive systems or read across. However “potential” might be too broad a definition for regulatory purposes. It was highlighted that the words “, or (sub)populations” were unnecessary. The Committee’s proposed definition for an endocrine disrupter was “an exogenous substance or mixture that has the potential to alter function(s) of the endocrine system and consequently cause adverse effects in an intact organism, or its progeny”

32. Members considered each of a set of criteria that had been proposed should be required for a chemical to meet the definition of an endocrine disrupter:

i. “adverse effects to have been seen in one or more standard toxicity studies in which the substance was administered by a route relevant for human exposure.” – Members broadly agreed with this criterion, but they suggested that more detailed information might need to be taken into account – for example the quality of the studies, the form of the substance and its stability.

ii. “the adverse effect(s) believed to be related to endocrine disruption to be the lead toxic effect(s) in the study; or occurring at a dose level close to that at which the lead toxic effect was first seen.” – Members disagreed with this criterion as it did not take into account the possibility of endocrine effects at higher doses or the potential for additivity.

iii. “the adverse effect(s) believed to be related to endocrine disruption to have been produced at a dose at or below the relevant guidance value for the
application of Category 2 “Specific Target Organ Toxicity-Repeated Exposure, STOT-RE” classification & labelling.” – This was agreed.

iv. “a mode-of-action link between the toxic effects of concern and endocrine disruption to have been established.” – Members considered this to be reasonable although in practice data gaps would need to be taken into account.

v. “the effects seen in experimental animals to be judged to be of potential relevance to human health” – This was agreed.

33. Members agreed that the use of the four agreed criteria would make it possible to confirm that a substance was an endocrine disrupter for regulatory purposes. However the evidence required to conclude that a substance was not an endocrine disrupter would depend on the degree of certainty that risk managers required.

Item 6: Health Assessment of Endocrine Disrupting Chemicals – The Danish EPA report and time trends in exposure to phthalates – TOX/2010/16

34. Dr Dearman declared a personal specific interest in relation to recent funding from the phthalates industry and withdrew from the discussion.

35. At the February 2010 meeting, Members had been presented with a paper summarising a recent report by the Danish Environmental Protection Agency (EPA) titled ‘Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products’. At that meeting, the Committee welcomed the approach of studying total exposures from a range of different scenarios, and asked to see the full report where the calculation of the exposure estimates was described for each compound. The Committee also wished to review the endpoints used for each compound as the basis of the derived no effect level (DNEL). It had been noted that for some compounds, the total calculated exposures were above the DNEL. However, as assessment factors were used in deriving the DNEL, the Committee considered that the margin between the exposure and the minimum effect level in the critical study could still be substantial.

36. The Committee had also considered that it would be useful to obtain information on time trends in exposure to a selection of the compounds investigated. Some compounds had been withdrawn from use in certain applications, while the use of others was growing, and depending on their chemical properties, this could reduce or increase concerns about the risks of adverse effects.

37. Paper TOX/2010/16 provided the Committee with the requested information on the endpoints used to derive DNELs for each substance in the report’s risk assessment. The full Danish EPA report was attached at Annex A. With regard to time trends in exposure to endocrine disrupting chemicals, the paper gave information on phthalates (selected because this was a group of substances for
which the estimated exposures were higher than the DNELs) as a preliminary indication of the type of data available.

38. Concern was expressed that the comparison of exposure of 2-year old children with endpoints based on developmental changes resulting from *in utero* exposure might not be appropriate. This comparison was likely to over-estimate risk. It was noted that 2-year old children are exposed to phthalates from a variety of sources, in and out of the home, through the diet, and through contact with clothes and toys. The exposure calculation assumed high exposure to high concentrations of the chemicals by each route, which represented an extreme worst case. One study noted high exposure through the use of baby lotion, and it was suggested that it might be possible to identify individuals at risk of high exposure.

39. Members commented on the time trends data. It was noted that 2003 was the last year for which there were data, and Members agreed that it would be useful to know the present situation, as there had been many changes in usage of the chemicals concerned. To assess the validity of the modelled exposure levels, it would be helpful if they could be compared with biomonitoring data. There were no UK biomonitoring data, but it was possible that such data were available from NHANES. This could be considered in a future COT discussion paper on the use of NHANES data.

40. Data from Scandinavia on exposure from rubber clogs had been tabled. It was unclear how relevant these would be to the UK, and uncertain exactly how the exposure had been estimated - in particular, whether the calculation had been based on the surface area or on the whole clog by weight.

41. It was asked whether the anti-androgenic effects noted in the study of DBP by Lee *et al.* (203, 221-238, 2004) represented a useful endpoint by which to assess endocrine disruption. The findings suggested some sort of endocrine activity was occurring but it was unclear whether it was an adverse effect. The DNEL derived from these data was very much lower than the chronic oral Reference Dose (RfD) set by the US EPA in 1990, which was now quite old. Members asked to see the paper of Lee *et al.* (2004). It was understood that DBP had been prioritised for assessment under the REACH legislation but a list of the highest priority substances had not yet been published and so it could be 2-3 years before any work was completed.

42. The phthalates had been selected as an example because of the reported high risk characterisation ratios in the Danish report. Members agreed that, before deciding whether more detailed consideration was required for other substances covered in the report, it would be best to wait for the results of studies being conducted under the EU Framework Programme and a report on mixtures of endocrine disrupting chemicals being prepared for the European Commission.

**Item 7:** T01045 – Assessment of joint endocrine effects of multi-component mixture of food contaminants and additives – TOX/2010/17 *(RESERVED BUSINESS)*
43. During the horizon scanning session at the COT meeting in February 2010 Members saw some interim reports from a project entitled 'The Assessment of Joint Endocrine Effects of Multi-Component Mixtures of Food Contaminants and Additives' (contract number T01045) with proposals for additional work. At that time, they indicated that they would like to comment upon the final report. Members now considered a draft final report of the work, which was funded by the Food Standards Agency under the T01, Risk Assessment Programme. Drs Sybille Ermler and Richard Evans from the School of Pharmacy were in attendance to answer questions relating to the research and its outcomes. This report was discussed as reserved business since it was not yet in the public domain. The full minute of this item will be released after the results have been published.

**Item 8: Use of Toxicogenomics in Toxicology – Design, analysis and statistical issues – TOX/2010/18**

49. A summary of paper TOX/2010/18 on the design and analysis of, and statistical issues associated with, toxicogenomic (TGX) work was provided by the HPA Toxicology Unit at Imperial College London. The COT and its two sister committees, the Committees on Mutagenicity (COM) and Carcinogenicity (COC) of Chemicals in Food, Consumer Products and the Environment had previously jointly considered TGX in 2002\(^1\) and 2004\(^2\). TGX methodologies had also been discussed at the COT Workshop on 21\(^{st}\) Century Toxicology in 2009\(^3\). The Chairman welcomed Dr David Lovell (Committee on Mutagenicity) who had produced the above 2004 paper on TXG for the committees, and had kindly agreed to attend and contribute to discussions.

50. Members recognised the substantial developments in TGX since 2004. It was agreed that paper TOX/2010/18 was a good summary and that future COT papers in this area might need to focus on sub-sections of the TGX field. Paper TOX/2010/18 was a comprehensive summary of array-based TGX approaches and was not intended to cover all TGX methodologies. Over coming years it was anticipated that the COT would see increasing numbers of papers describing the use of TGX to investigate chemical toxicity. In particular, research areas such as low dose effects, pattern matching, margins of exposure and human relevance were expected to make greater use of the technology. It was therefore important for the Committee to be able to evaluate TGX data critically.

51. The Committee noted that selecting the sample size for a TGX study is a fundamental step regardless of the type of study to be undertaken, and that it requires a power calculation. It was considered particularly important for microarray experiments to include a sufficiently large baseline group in order to characterise the noise associated with normality in comparisons with later time points. In relation to the statistical power of TGX studies to detect changes, it was observed that some researchers had moved towards statements along the lines of “there is an X% chance that these Y% of gene changes represent the most significant differences

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\(^3\) [http://cot.food.gov.uk/pdfs/cotstatementwkshp200903.pdf](http://cot.food.gov.uk/pdfs/cotstatementwkshp200903.pdf)
across the classes” and away from less informative phrases such as “these are the most significant changes (P = 0.05)”.

52. Many studies were thought by Members to be under-powered. However, it was recognised that there is some tradeoff between power and feasibility. In relation to dose selection, an example was given that if RNA responses to an intervention in laboratory animals were sought, then the merits of pushing exposures up to the point at which signs of toxicity were apparent would be questionable. A Member asked whether meta-analyses of ‘under-powered’ studies had been undertaken. Although such data-mining was a growth area in metabonomics, it was felt that it may be of limited value at this time. Differing approaches to normalisation were considered a challenge in such meta-analyses.

53. The rationale for selection of time points for temporal studies was not always clear, but this needed to be considered in advance since TGX responses at the genomic, transcriptomic and metabonomic levels are expected to occur at different time points after intervention.

54. It was noted that some individuals still advocated that the pooling of biological material from multiple biological sources was acceptable under exceptional circumstances (e.g. in order to meet analytical requirements). But in general, the Committee agreed that pooling, which prevents an assessment of inter-individual variability, should be avoided.

55. It was felt that the progress over recent years in the standardisation of analytical platforms for TGX across laboratories and platforms represented a major improvement since the last Committee review in 2004.

56. Another consideration was the extent to which data processing (e.g. normalisation) was concordant between the various companies producing and supporting TGX platforms. It was noted that in the application of TGX to study of Streptomyces, just one manufacturer produced all the TGX chips used worldwide, which facilitated standardisation. This could offer a model for other fields.

57. The Committee also discussed the selection of statistical approaches, and reporting of results from different statistical approaches, in the identification of, for example, differentially expressed genes. Members considered that ideally the statistical methodology should be defined at the outset of a study, based on an a priori hypothesis, and informed by the study objectives and study protocol. It was noted that after data had been acquired, it was common for authors to try a range of statistical approaches (e.g. different forms of supervised analysis). It was considered likely that researchers would eventually find a separation of datapoints when trying multiple multivariate models, due to the massive numbers of datapoints and variety of a priori assumptions underlying the different models. In such cases, rather than just pick the ‘best’ results; researchers should fully report the chemometric steps that they had taken.

58. Members requested a paragraph in the draft statement on the implications of Bayesian statistics and a description of the limitations of different statistical approaches used in TGX. TGX datasets typically contain many thousands of
variables and a much smaller number of samples, but it was felt that on some occasions, even when an author claimed to have corrected for multiple testing, that was not the case. Additional text covering replicates was requested. A lack of consistency was noted in the usage of and definitions for false discovery rate (FDR) and multiple comparisons in different TGX software. The paper contained a summary of different TGX-specific databases, and it was noted that there were a large number of differing standards, which in some cases were conflicting. Consideration of systematic and stochastic variation in genes (the latter arising from random events at a molecular level such as whether a cell mutates or dies in response to a genotoxic insult) would also be useful.

59. Members noted that when the Committee critically reviews TGX papers as part of an assessment of a chemical, it will need to look beyond what may be a very narrow focus of a paper in order to interpret the results. There is a continued need to look for third-party confirmation of findings and support (e.g. other types of study or phenotypic anchoring) and for consideration of plausibility and human relevance of data.

60. The Chairman thanked Dr Lovell for assisting the Committee. It was agreed that the Secretariat would begin to draft a statement. This should be short and relevant to the Committee’s role. Further papers on this topic, including applications in risk assessment, would be presented to COT for discussion at future meetings.

Item 9: FSA funded project on expression of uncertainties in risk assessment – TOX/2010/19

61. This work was funded by the Food Standards Agency under the T01, Risk Assessment Programme and addressed uncertainty. Professor Coggon and Professor Boobis declared personal specific interests as they were advisors on the project.

62. As part of the research contract, the COT had held a Workshop on February 3rd 2010, at which COT Members and invited guests participated in discussions exploring the evaluation and expression of uncertainties in risk assessment. Participants had looked at examples of risk assessments previously considered by the Committee and used a draft framework to consider whether this could make the steps of the risk assessment process easier, and the risk assessment process more transparent. The Committee had discussed a draft report of the workshop at its 4th May meeting. Paper TOX/2010/19 contained a near final draft of the report on the project.

63. Members considered that the draft report reflected the comments and consensus reached at the workshop and had generally responded to points raised previously. Members reiterated that they were less keen on the use of numerical values or symbols to express uncertainty about qualitative conclusions, but accepted that the report reflected the discussion on these points. Members acknowledged that any system whether verbal or numerical could be misinterpreted but felt that the process had moved forward significantly.
64. The Chair indicated that he had heard from a representative of a Non-Governmental Organisation who had noted the papers on the website and thought the approach would be helpful and was generally positive despite some reservations over the language used.

65. It was noted that the structure of the report should now be adjusted to address qualitative before quantitative approaches since the original rationale for their order no longer applied. The proposed approach to evaluating uncertainty when applying uncertainty factors was an attempt at practicality but it was unlikely the criteria would often be met fully.

66. Members were informed that the report would be finalised and submitted to FSA, and that the Secretariat would pilot the approach in relation to one or more future topics considered by the Committee. The Chairman would report to GACS on the work as other committees were interested in the approach.

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67. Members were advised that it would be possible to obtain more details if required and noted that the COC paper on the assessment of risks from combined exposures to chemical carcinogens was available on the COC website.

Item 11: Any other business

68. Dr Benford advised Members on the initial impact of the recent budget on administrative COT costs, which included:

- First class train travel should not be used unless it is the cheapest option
- Hotel costs have been capped
- The COT annual report will not be published in paper form; it will be available on the web as in previous years
- An Out of Town meeting will not be held in February 2011, although a two day meeting could be held in London if an appropriate topic was identified for a symposium or workshop on the second day.

Item 12: Date of next meeting

69. The next meeting of the Committee would take place on Tuesday, 14th September 2010 at Aviation House.