

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

Minutes of the meeting held on Tuesday 14 February 2006 at the Moat House Hotel, York

Present

Chairman                    Professor Hughes

Members:                    Dr Bell  
                                   Professor Boobis  
                                   Dr Carthew  
                                   Dr Jackson  
                                   Professor Lunec  
                                   Professor Ray  
                                   Dr Rushton  
                                   Dr Stanley  
                                   Ms Ward  
                                   Ms Williams

FSA Secretariat:        Dr Benford                    (Scientific Secretary)  
                                   Dr Gott  
                                   Ms Mulholland  
                                   Mr Maycock  
                                   Dr Rajapakse  
                                   Ms Cleaver  
                                   Dr Thatcher  
                                   Dr Creton  
                                   Ms Aisbitt

HPA Secretariat        Mr Battershill

Assessors	Dr Dyer	DH
	Dr Hosford	EA
	Mr Ridgeway	HSE
	Mr McManus	PSD
Other officials in attendance:	Dr Damant	FSA Scientific Data Quality Branch – item 7
	Dr Hargin	FSA Fish and Shellfish Hygiene Branch – item 7
	Dr McElhiney	FSA Scotland – item 7
	Mr McDougall	FSA Scotland – item 7
	Dr Dicks	FSA Scotland – item 7
	Ms Wright	FSA Scotland – item 7
	Mr Whelan	FSA Press Office
	Dr O’Leary	DH Toxicology Unit – item 5

Observers

Dr Edwards	HPA
Dr Hetherington	HPA – item 4
Dr Anderson	Home Office – item 7
Dr Dennison	Home Office – item 7
Mrs Wilder	PSD – item 4
Mr Hamey	PSD – item 4
Ms Kennedy	PSD – item 4
Ms Rogers	PSD – item 4
Ms Downs	UK Pesticides Campaign – item 4
Dr Lees	CEFAS – item 7
Dr Irving	CEFAS – item 7

Draft

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## Announcements

1. The Chairman, Professor Hughes, welcomed Members and other attendees to the meeting. Members were reminded to declare any commercial or other interests in any of the agenda items.

### Item 1: Apologies for absence

2. Apologies for absence were received from Dr Hinson, Professor Strobel, Dr Dearman, Dr de Vries, and Professor Rowland.

### Item 2: Minutes of the meeting held on 6 December 2005 – TOX/MIN/2005/06

3. The minutes of the 6 December meeting were agreed subject to the following amendments (in italics):

- Delete Dr Gott from list of attendees
- Para 12, line 5: Insert *method* as final word of sentence.
- Para 17: Final sentence to read: *Members noted that limited clinical chemistry and no urinalysis had been conducted and that the apparent lack of dose response for effects was very unusual for a toxic substance in a sub-chronic study.*
- Para 18: Change to: *It was agreed that the study was therefore difficult to interpret and ideally the slides should be re-read.*
- Para 19: Final sentence to read: *Effects during pregnancy were not considered relevant for exposure to formula fed infants.*
- Para 27, final line: ...were associated with *only* minor side effects.
- Para 28, line 5: ...in general, *these studies* considered only...
- Para 34, line 2: The decision to ban kava *kava*...
- Para 40: First sentence to read: *It was considered that there was sufficient evidence to conclude a mechanism of action similar to that of their chlorinated analogues, via...*
- Para 40, line 3: ...Assuming *dose* additivity
- Para 40, line 5: ...more protective than *assuming*...

- Para 41: Final sentence to read: *Therefore, for the brominated congeners where it is not appropriate to set TEFs for the chlorinated congeners, it may be necessary to use comparison of concentrations with NOAELs/LOAELs from toxicity studies, if available.*

### **Item 3: Matters arising**

4. The Chairman noted that Professor Ashby and Dr Rylance had resigned from the Committee and invited Members to make recommendations for candidate replacements.

### **Item 4: Royal Commission on Environmental Pollution (RCEP): Crop spraying and the health of residents and bystanders – TOX/2006/01**

5. This item had been referred to the COT and the COC by the Advisory Committee on Pesticides (ACP) and DEFRA. The COT and COC had been asked to provide toxicological advice on the report published by the Royal Commission on Environmental Pollution (RCEP) on crop spraying and the health of residents and bystanders. In attendance were scientists from the Pesticides Safety Directorate (PSD), Mrs Jayne Wilder and Mr Paul Hamey, and one public observer.

6. The RCEP report was published in September 2005. The ACP had published a statement in response to the RCEP report on 6 February 2006. Members had been provided an internet link to the ACP statement, but were reminded of the need to consider the issues in the RCEP report independently.

7. Members were provided with the full RCEP report in addition to a number of papers cited by the RCEP in connection with development of animal models for Chronic Fatigue Syndrome (CFS), an overview of the risk assessment process for bystanders, information on current arrangements for post-market monitoring and reporting of adverse effects attributed to pesticides, guidance provided by DH to GPs on the assessment of chronic ill health linked to pesticide exposure and an example copy of a Pesticides Incident Appraisal Panel (PIAP) report.

8. Members were asked to particularly focus on Chapter 2 of the RCEP report dealing with toxicological aspects and the approach to risk assessment for bystanders, and to comment on the overall conclusions and recommendations where possible.

9. General comments were initially sought. Members were pleased that the subject had been reviewed were disappointed with the way evidence had been presented in the report, which it was felt diminished the content. The Committee considered Chapter 2 section by section.

*Paragraphs 2.1-2.15: Introduction, health effects attributed to pesticides, acute effects, chronic health effects*

10. It was considered that level of exposure was critical and it was suggested that exposure of bystanders and residents would be significantly lower than for operators, even taking into account use of personal protective equipment by operators. A PSD representative agreed, noting that US studies of farm workers and their families had shown exposures of the non-pesticide operator members of the families to be around one order of magnitude less than for the operators. In addition, biomonitoring data from the US had indicated that exposures of bystanders and residents are lower than predicted by exposure models used as part of the risk assessment process. Members considered identification of adverse effects in operators to be a useful model for bystanders and therefore there was reassurance regarding the potential for adverse effects in bystanders.

11. It was considered that the only possible organic factor which could explain ill health in exposed bystanders which did not occur in operators was a particular susceptibility in some bystanders. It was noted that although operators could be considered to not represent the full heterogeneity of the general population, the systemic acceptable operator exposure level (AOEL), which was used in risk assessment for both operators and bystanders, incorporated an uncertainty factor to account for inter-individual variation in the general population and was an appropriate approach for risk assessment of bystanders and residents.

12. Given the heterogeneity of bystanders and their low level of exposure compared to occupationally exposed groups, it was considered that there was little merit in undertaking epidemiological studies in bystanders as a group, and that a more appropriate approach would be to investigate genetic and phenotypic characteristics in individuals with self-reported chronic illhealth. Such an approach would be required to identify the cause of this disease, and if there was any increased susceptibility in some individuals.

13. Members agreed with an RCEP conclusion of this section that no firm conclusion could be drawn that pesticide exposure was causing ill health experienced by bystanders and residents. It was noted that there was a lot of speculation in this part of the report. It was also noted that possible psychological factors had been raised but that these were not referred to in the overall conclusions of the report.

*Paragraphs 2.16-2.19: Mechanisms of action of pesticides and possible targets in humans*

14. Members were not aware of any evidence to suggest that conventional dose-response assessment of toxicological effects was not appropriate. It was noted that there was ongoing Government research on organophosphates, and that this supported the principle that response depended on dose. Members considered that this section confused hazards with risks and observed that throughout the report there was a reference to a need to prove

the absence of effects; Members considered that it was not possible to prove a negative but that instead there was a need to consider the probability of effects based on exposure and biology. It was considered that the probability of low dose effects from organophosphates and pyrethroids was extremely low. Members considered this section to be limited and observed that there were many classes of pesticides other than organophosphates and pyrethroids which had not been considered here.

*Paragraphs 2.20-2.26: Epidemiology*

15. It was noted that a limitation of epidemiological studies in relation to pesticides was the imprecise exposure assessment, with often a complete lack of quantitation. Thus the Institute for Environment and Health review of studies on Parkinson's disease had insufficient data available to identify individual pesticides; the best descriptor available was groups such as herbicides. Where associations were found it was not possible to relate them to dose. A key difficulty was the retrospective evaluation of exposure using self-reported questionnaires. Improvements in study design were required in this respect.

16. Members observed the comparison in the RCEP report of the air quality standard for nitrogen dioxide and the relevant occupational standard. It was noted that the AOEL used in pesticide risk assessment incorporated an uncertainty factor to incorporate the variability in the overall general population.

17. It was noted that some references to information that had not been peer-reviewed were quoted. Whilst information from non-peer reviewed sources could be valuable as long as an attempt to assess the quality of the data had been made, it was noted that it was difficult to identify or source some of the references in the RCEP report, so they could not be checked.

*Paragraphs 2.27-2.34: Review of epidemiological studies*

18. Members considered that the review of epidemiological studies had been limited and that a more substantive review of the literature should be undertaken. Members noted that the RCEP did not come to any conclusion as to whether pesticide exposure was causing illhealth. It was suggested that one possible way forward would be to consider para-occupational exposure, e.g. spouses and children of farmers who might have exposures above that of bystanders. It was noted that the American Farm Survey of Occupation might be one useful source, but a literature review should identify other relevant research projects. It was noted that such data did not necessarily establish cause and effect.

19. Members were aware of the difficulties in undertaking such work relating to many sources of exposure to pesticides and the many different types of pesticides in addition to potential exposures resulting from spray activities. Thus, for example, preliminary information from an investigation of

people attending GP surgeries showed that 45% of them had used some form of pesticide in the domestic environment in the week before consultation.

20. It was noted that the RCEP report referred to clusters of ill health, but that clusters were not evidence of causation, and that a hypothesis of a minority of bystanders with heightened susceptibility was unlikely to fit with an area-based cluster pattern of ill health.

*Paragraphs 2.35-2.39: Multisystem disease (chronic fatigue syndrome, multiple chemical sensitivity)*

21. Whilst the reports of ill health in association with residence near to fields treated with pesticides involved a wide range of signs and symptoms, some were probably related to multiple chemical sensitivity (MCS). It was considered that there were two schools of thought with regard to MCS, that it was either psychological in nature or organic. If the latter, this indicated a particular vulnerability in some individuals that would be susceptible to experimental investigation. It was noted that the literature indicate that two important factors in the reporting of ill health by persons reporting ill health in response to very low chemical exposures were odour, which may not reflect exposure to an active ingredient, and the involuntary nature of exposure. These suggested that psychological factors may be an important component in the condition.

22. Members agreed that chronic fatigue syndrome was a medically defined condition. However, multiple chemical sensitivity was not a clearly definable medical condition and the differences between multiple chemical sensitivity and chronic fatigue syndrome were unclear. There were a number of similarities in reported symptoms, however not everyone with chronic fatigue syndrome reported sensitivity to chemicals.

23. Members heard that there were a number of papers identified in the literature since the COT's last consideration of multiple chemical sensitivity in 2000, and agreed that these could be reviewed. This work might also involve reviewing chronic fatigue syndrome.

24. It was agreed that a fundamental research programme into multi system disease involving research councils and the Department of Health as recommended by the RCEP was not warranted. With respect to chronic fatigue syndrome it was considered that there could be merit in investigating individuals with chronic fatigue syndrome who believe their condition is due to prior infection in comparison to those who believe it is due to chemical exposure. Members commented that investigations using brain imaging techniques needed to incorporate appropriate controls. It was noted that even symptoms with a psychological origin could give rise to changes observable in brain imaging.

*Paragraphs 2.40-2.53: Toxicology*

25. Members considered that there was no rationale for developing animal models to test for poorly-defined spectrum of human health effects described in the RCEP report without a clear mechanistic rationale for undertaking such work. One difficulty was the possibility of a psychological component in conditions such as chronic fatigue syndrome and multiple chemical sensitivity, which meant that some type of stress factor may need to be incorporated into any such model. Another was that the majority of the symptoms reported are subjective. Members had difficulty in identifying the value of in-vitro techniques to investigate such complex multi-functional ill-health effects with poorly defined causation.

26. It was agreed that the Functional Observational Battery, now in common use in rodent 90-day studies, was capable of identifying some of the toxicological symptoms which are reported in chronic fatigue syndrome, though it was not possible to relate these symptoms to chronic conditions such as chronic fatigue syndrome. Members considered that there was little value in using *in vitro* techniques to investigate such chronic ill health effects.

*Paragraphs 2.54-2.64: Monitoring*

27. Members noted that the majority of approved pesticides are eliminated quickly once absorbed, and therefore biomarkers are short-term. Levels of any biomarkers may relate more to time of exposure rather than dose, making calibration difficult.

28. The RCEP report had advocated large-scale studies such as the National Health and Nutrition Examination Survey (NHANES) in the US. Members considered that such programmes of work provided large numbers of results which were difficult to interpret. Members agreed that it was important to consider potential biomonitoring studies, but considered that small scale focused prospective studies using pesticides for which there was good knowledge of kinetics in humans was preferable. Such studies would form the basis for extrapolating to potential bystander exposure to other pesticide active ingredients.

29. The Committee heard information on the studies instigated by PSD relating to permethrin and chlorpyrifos and agreed the proposed research would fulfil the COT suggestions for biomonitoring. Members noted the difficulties in undertaking such research such as sampling, storage, analysis and obtaining ethical consent for participation. In addition, it was questioned whether the biomarkers would be sufficiently sensitive to detect exposure in bystanders. Members noted that if biomonitoring was routinely used in data packages for pesticides then there would be a method for comparing data with that derived from toxicological evaluation in animal studies.

*Paragraphs 2.65-2.69: Recommendations: human health*

30. The Committee did not consider that there was a basis to support the recommendation that there was an urgent need for research (paragraph 2.65). It was agreed that recommendations relating to additional precaution in

risk assessment above the already precautionary approach used did not have a scientific basis but related to policy regarding pesticide approvals. Regarding the recommendation in paragraph 2.66, Members agreed that the work they had recommended on para-occupational exposure and a review of chronic fatigue syndrome and multiple chemical sensitivity regarding evidence for susceptibility were required. Regarding paragraph 2.67 Members agreed that specialist investigations should be aimed at all potential causes of chronic illness such as chronic fatigue syndrome and multiple chemical sensitivity, not just the proposed hypothesis relating to bystander exposure to pesticides. In relation to paragraph 2.68 the HPA agreed to consider the advice the Committee had provided on biomonitoring.

*Paragraphs 2.70-2.96: Health effects, monitoring and reporting*

31. Members noted that the COT had no previous involvement in monitoring for adverse effects attributed to pesticides. It was agreed that the generic advice for further involvement of primary care would be difficult to undertake and that the RCEP had not considered the diversity of ways in which primary care is delivered. Members considered that most general practitioners would not have the time to consider the causes of the mainly ill-defined symptoms individuals may present with.

32. Members agreed the advice published by DH in 1996 regarding advice to general practitioners with suspected ill health attributed to pesticides was inaccurate as it did not allow for all causes of illness to be investigated.

33. The Committee agreed that remaining questions listed in the COT paper had been answered in the course of discussing Chapter 2 of the RCEP report, and had no further comments. It was agreed that a joint COT/COC statement would be drafted following the consideration by the COC.

34. In response to the chairman's invitation for comment from observers, Ms Georgina Downs of UK Pesticides Campaign made a statement. She did not agree the summary produced by the secretariat and her comments on this item are therefore published separately.

**Item 5: Update review of toxicology literature on the topical insect repellent N,N-diethyl-m-toluamide (DEET) – TOX/2006/03**

35. The COT considered a review of the available literature at its meetings from February to July 2002. The committee agreed to keep DEET under review and a number of recommendations were agreed by members. These were as follows:

- Information on exposure should be made publicly available
- Additional animal studies are required to verify the neuropathological effects seen in repeat dosing dermal studies of DEET in rats

- The Department of Health should undertake further monitoring for reports of adverse effects associated with exposure to DEET
- Consideration should be given to undertaking epidemiological studies
- Industry should seek to attain a consistent approach to labelling through voluntary action.

36. Members agreed that these recommendations were still relevant and then discussed the evidence that had become available since the previous discussion in 2002.

37. In looking at the new human case reports which had been collated from information provided by the National Poisons Information Service Centres (NPIS), the Hospital Episode Statistics (HES) and the Hospital Accident Surveillance Scheme (HASS), members were reassured that the effects were relatively minor and did not include any cases with overt neurotoxicity. The small number of cases when compared to the estimated high usage of DEET was also reassuring, but it was agreed that there were no precise data for the U.K. in this regard.

38. Members were informed that DEET was being considered as part of the EU review scheme under the Biocide Products Directive. It was possible that the COT review could be forwarded to the rapporteur Member State. It was noted the EU review would provide information on usage and would also allow for consistent labelling to be applied to DEET products.

39. Members had a number of questions regarding the studies on absorption of DEET when used concurrently with sunscreen on mice and piglets. They were concerned that use of sunscreens may alter the degree of dermal absorption of DEET when compared to DEET used alone. It was estimated that the margin of safety for DEET might be reduced following co-exposure to DEET and sunscreen. The secretariat stated that they would request further information from the DEET Joint Venture Group, which had indicated that additional dermal; absorption studies were available.

40. The new neurotoxicity studies were reviewed and members commented that the neuronal effects attributed to DEET in some of the studies might be due to artefacts caused by incorrect handling of the brain tissue after the death of the animal. Members expressed concern that the observed eosinophilic degeneration of neurones might actually be basophilic post mortem changes. However if there were significant microglial and astrocytic reaction to neuronal damage, it was possible that the observed lesions occurred in-life. Members considered that Professor Abou-Donia should be asked to comment on this observation and a number of questions relating to methods of the study. It was noted that the secretariat would be meeting Professor Abou-Donia on 22 February where appropriate questions could be provided for him.

41. The new genotoxicity data were noted and members concluded that given the totality of mutagenicity data, there was no requirement for the assessment of DEET to go to the COM. The secretariat noted that the unusual approach given to score DNA damage in this assay precluded an evaluation of the results.

42. Members stated that the human studies available were fairly difficult to interpret and the effects observed would be difficult to separate from sunstroke. It was agreed that the DEET Joint Venture group should be asked whether there were any poisoning case-report from the U.S.A. which referred to co-exposure to DEET and sunscreen.

#### **Item 6: Organic chlorinated and brominated contaminants in fish – TOX/2006/02 and TOX/2006/09**

43. At the meeting in December 2005, COT discussed paper TOX/2005/36 that reviewed the toxicology of the polybrominated dioxins (PBDDs), furans (PBDFs) and biphenyls (PBBs). Advice from the Committee was that toxic equivalency factors (TEFs) developed for the chlorinated dioxins, furans and dioxin-like polychlorinated biphenyls (PCBs) could be used to provide a preliminary indication of the dioxin-like activity of the PBDDs, PBDFs and dioxin-like PBBs.

44. In January 2006 Members considered paper TOX/2006/02 by correspondence. This paper summarised the results from a number of surveys recently completed by the Food Standards Agency. Farmed and wild fish and shellfish consumed in the UK, and the 2003 and 2004 total diet study (TDS) samples have been analysed to determine the concentrations of a number of organic contaminants: chlorinated dioxins and dioxin-like PCBs, brominated dioxins and dioxin-like PBBs and brominated flame retardants. The surveys provide data on the levels of these contaminants in a broader range of fish species than previously available.

45. Where comparison was possible, concentrations of chlorinated dioxins and dioxin-like PCBs in fish had decreased. Comments received by correspondence from Members indicated that the new data did not suggest a need for a change in the FSA's current advice on consumption of oily fish. However, in regards to the use of the chlorinated TEFs for the brominated dioxin-like compounds it was felt that the uncertainties associated with this approach to combining the data from the brominated contaminants needed to be clearly acknowledged.

46. The Chairman thanked Members for corresponding comments on TOX/2006/02 and asked them to consider the first draft working paper (ANNEX A of paper TOX/2006/09) with an aim to agreeing the draft conclusions. This paper summarised the survey results, COT's previous evaluations and the Member's views as expressed by correspondence.

47. The finding that concentrations of dioxins and dioxin-like polyhalogenated biphenyls in some species of non-oily fish were similar to those commonly found in some oily fish was considered significant, given that some species, e.g. sea bass, were increasingly consumed as part of the UK diet. It was noted that the presentation of contaminant levels separated into oily and non-oily fish species appeared artificial. A Member commented that more consideration should be given to presenting the potential risks from combined weekly consumption of oily with non-oily fish. It was acknowledged that contaminant levels in non-oily fish species, not previously surveyed, complicated the current FSA advice that provides general guidance based on oily and non-oily fish consumption rather than identifying specific species of fish of concern. Given the new data on dioxin levels in non-oily fish it was not considered feasible to provide simplistic advice along the lines of the current guidance. Advice should seek to ensure people do not regularly consume two portions of the six more contaminated species of non-oily fish in addition to the recommended weekly oily fish consumption.

48. A Member asked whether there was any difference in bioavailability of the contaminants between the oily and non-oily species of fish and whether this might impact on the risk assessment. The secretariat was not aware of any data relating to this concern. It was also considered unfeasible to formulate advice on the consumption of these six species of non-oily fish on the basis of an analysis of the nutritional benefits and possible risks to health.

49. The Committee agreed the conclusions, subject to further consideration of the advice on consumption of certain species of non-oily fish and shellfish taking into account nutritional as well as toxicological issues.

50. It was suggested that, given the substantive evidence indicating that levels of the dioxin-like contaminants are decreasing with time, these new data did not indicate a real public health issue. The conclusions were precautionary on the basis that data were now available for additional contaminants and for a wider variety of fish species than previously, rather than there being an increased exposure to dioxin-like compounds. It was, therefore, agreed that the final conclusion was particularly pertinent:

- *There are considerable uncertainties in the data which indicate that this assessment might be over-precautionary. The risk assessment could be improved by refinement both of exposure assessment and of the toxicological basis for the TEFs, using probabilistic approaches. Modelling the available information may help to determine where the greatest uncertainty lies, in order to prioritise future research.*

#### **Item 7: Risk assessment and monitoring of marine biotoxins in support of public health – TOX/2006/04**

51. In December 2005, the Committee considered paper TOX/2005/35 on the risk assessment and monitoring of marine biotoxins in support of public health. Members were presented with information relating to several classes

of biotoxins, but discussion focussed on the toxins responsible for paralytic shellfish poisoning (PSP).

52. PSP is a neurotoxic syndrome with symptoms including tingling and numbness of extremities, respiratory distress and muscular paralysis leading to death by asphyxiation. The toxins responsible for PSP are saxitoxins (STXs), of which there are around 20 known analogues.

53. In 2004, an FAO/IOC/WHO Expert Consultation established a provisional acute reference dose for dietary intake of PSP toxins that could be ingested in a period of 24 hours or less without appreciable health risk. A value of 0.7 µg STX equivalents (eq)/kg bodyweight (bw) was derived from a provisional lowest observed adverse effect level (LOAEL) of 2 µg STX eq/kg bw identified from epidemiological studies, and a safety factor of 3. At the December COT meeting, members requested further details on the epidemiological data for PSP toxins in order to comment on the appropriateness of the proposed acute reference dose. This information was presented to the Committee in TOX/2006/04.

54. A number of uncertainties in the human data were noted, relating to inaccuracies in exposure assessments due to differences in sampling and analysis of contaminated shellfish at the time of poisoning incidents, and uncertainties with respect to amounts consumed. In the majority of studies PSP toxin levels in the shellfish were calculated using a mouse bioassay (MBA).

55. It was noted that some PSP cases had been reported following consumption of PSP toxins below the FAO/IOC/WHO's provisional LOAEL of 2 µg STX eq/kg bw. Relatively few patients had been ill after consuming such amounts, and FAO/IOC/WHO had considered that mild cases had generally consumed 2-30 µg STX eq/kg bw, while more severe cases involved an exposure of >10-300 µg STX eq/kg bw. Given the limitations regarding the exposure data, the Committee concluded that the FAO/IOC/WHO approach was reasonable.

56. The Committee also discussed the safety factor that had been applied to the LOAEL by FAO/IOC/WHO. A safety factor of 3 had been applied to the LOAEL cited for mild effects. The value of 3 had been selected because the epidemiological data on PSP represented a wide range of individuals with varying susceptibilities, and because mild illness is readily reversible. In addition, members noted that the reported dose range was likely to represent individuals at the extreme ends of sensitivity. The Committee noted that the proposed acute reference dose was about one-tenth of the lower end of the dose range associated with severe illness and was therefore not likely to be overly conservative. The Committee concluded that the acute reference dose proposed by FAO/IOC/WHO was appropriate for protection of public health.

57. Members noted that a portion size of 250 g was a reasonable estimate for high level consumption in the UK. An intake of PSP toxins at the acute reference dose of 0.7 µg STX eq/kg bw would result from consumption of

250g of shellfish containing 17 µg STX eq/100 g shellfish meat by a 60 kg adult. Rounding up to a single significant figure indicated that 20 µg STX eq/100 g shellfish meat would be the maximum concentration considered to be without appreciable health risk.

58. A member noted that the current regulatory limit for PSP toxins in shellfish is 80 µg STX eq/100 g shellfish meat, which could result in some individuals consuming greater than the proposed acute reference dose. There had been no incidents of PSP resulting from consumption of UK shellfish since the official UK monitoring programme was introduced. This could be interpreted as suggesting the current regulatory limit may provide adequate protection for human health. However, the Committee agreed that that it would be imprudent to conclude that mild cases of PSP have not occurred in the UK, as they may go unreported. Furthermore, given the potential for PSP to result in severe illness or even death, the proposed acute reference dose should not be ignored.

59. An MBA, involving intraperitoneal injection of shellfish extract, is currently used in the UK PSP monitoring programme. A range of alternative methods for detection of PSP toxins has been developed, including high performance liquid chromatography (HPLC) and an immunoassay known as the Jellett Rapid Test (JRT). At the December meeting, members had requested clearer information relating to the performance characteristics of these three methods, and this was also included in TOX/2006/04.

60. The limit of detection for the MBA is approximately 30-40 µg STX eq/100 g shellfish meat. An HPLC method developed by Lawrence *et al.* (*J AOAC Int* 87, 83-100, 2004) has recently undergone interlaboratory validation and has a substantially lower detection limit than the MBA currently employed. The JRT is not a quantitative assay and has been used to screen out samples containing less than approximately 40 µg STX eq/100 g shellfish meat.

61. The Committee noted that HPLC was currently the only method adequate to detect PSP toxins at the concentration of 20 µg STX eq/100 g shellfish meat, identified as necessary for protection of public health. It was recommended that HPLC be used for quantification of PSP toxins subject to appropriate quality control measures and method validation in the testing laboratories, including investigation of possible interfering peaks for different matrices. Further comparative testing against the MBA was not considered to be necessary.

62. Officials present expressed the view that it might be possible for the JRT to be re-engineered to detect lower concentrations of PSP. The Committee agreed that if this was possible it could be used as a screen, using HPLC for quantification of positive results.

63. At the current regulatory limit of 80 µg STX eq/100 g shellfish meat, the Committee considered that the JRT could be used to screen out samples containing approximately =40 µg STX eq/100 g shellfish meat, and to identify

samples containing approximately =40 µg STX eq/100 g shellfish meat for quantitative testing.

64. The Committee agreed that it would be appropriate review its advice once new data on the distribution of PSP toxins in UK shellfish become available from the more sensitive HPLC tests.

#### **Item 8: Potential future discussion items – horizon scanning – TOX/2006/05**

65. Paper TOX/2006/05 described ongoing topics as well as known and possible items that the Committee may be asked to consider during 2006.

66. The following papers were to be finalised:

- COT statement on combined use of 2-chlorobenzylidene malonitrile (CS) and PAVA (Nonivamide) sprays;
- COT statement on perfluorooctane sulfonate (PFOS)
- COT statement on perfluorooctanoic acid (PFOA)

67. Members were asked to send comments on these documents to the Secretariat.

#### *Agenda items for 2006*

68. Members were informed of the following future agenda items of which the Secretariat is aware:

- Cabin air quality and organophosphates
- Research on food additives and children's behaviour, funded by the Food Standards Agency
- Nickel in boiled water

#### *Furan*

69. An update on the COT/COM/COC conclusions was given. Following a research call from DG Research, comments were requested on research areas specific for UK consumers that should be considered for funding by the Food Standards Agency. Members were requested to send their comments to the Secretariat.

#### *Emerging issues*

70. Members' views were requested on emerging toxicological issues that are of relevance to public health or to Committee working procedures that should be included in the programme of work in 2006. These could be specific issues to be included as routine agenda items, focused topics for one-day open meetings or generic issues requiring the establishment of a working group.

71. It was suggested that the relevance of new approaches to risk assessment given by the WHO/IPCS should be considered.

72. With reference to the poor risk communication by the water authorities, shown in the Lowermoor Report, it was suggested that risk communication strategies be discussed. In addition, a one day meeting on risk analysis to be attended by the COT, COM and COC and possibly other committees was suggested.

**Item 9: First draft working paper on uranium levels in water used to reconstitute infant formula – TOX/2006/06**

73. The COT had discussed the health implications for infants of consuming formula reconstituted with water containing uranium at the WHO guidance level at the October and December 2005 meetings. A working paper had been drafted based on the discussions at these meetings.

74. Members were asked to send comments on the draft working paper to the Secretariat.

**Item 10: 2005 Annual report of the Committee on Toxicity – TOX/2006/07**

75. Paper TOX/2006/07 provided the draft text of the COT section of the 2005 COT/COM/COC Annual Report.

76. Members were asked to send comments on the report to the Secretariat.

**Item 11: Papers for Information**

77. Members were provided with the following papers for information:

- **Update on items previously discussed by the COT – TOX/2006/08**

**Item 12: Any other business**

78. There was no other business.

**Item 13: Date of next meeting**

79. Members were informed that the next meeting of the Committee would take place on Tuesday 28 March 2006 in Aviation House.