Scientific Advisory Committee on Nutrition &
COMMITTEE ON TOXICITY OF
CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT

FISH INTER-COMMITTEE SUB-GROUP
Aviation House, Conference Room 1
30th June 2003

Attendees
CHAIR: Professor Alan Jackson (SACN Chair)
Professor Ieuan Hughes (COT Chair)
Professor Kevin Chipman (COT)
Dr Timothy Key (SACN)
Professor Christine Williams (SACN)
Dr Diane Benford (COT secretariat)
Dr David Gott (COT secretariat)
Dr Alison Tedstone (SACN secretariat)
Dr Peter Sanderson (SACN secretariat)
Ms Angela Inwood (SACN secretariat)
Mr Nick Tomlinson (FSA-CST)

Apologies
Professor Ian Rowland (COT)
Dr Sheela Reddy (DoH)

Chair's introduction

1. The Chair outlined the purpose of joint committee meeting: to consider current advice on fish consumption, both the risks and benefits, and current dietary recommendations.

2. It was noted that Joint FAO/WHO Expert Committee on Food Additives (JECFA) had recently revised their provisional tolerable weekly intake (PTWI) for methylmercury (paper tabled) and that COT would have to consider this in due course.

Current advice and its basis

3. The FSA's advice on fish consumption (paper tabled), and supporting evidence, was described by the SACN and COT secretariats. The advice on fish consumption from other countries was described.

4. The FSA general advice on fish consumption, to consume at least two portions of fish per week, of which one should be oily, is based on the 1994 COMA report on the Nutritional Aspects of Cardiovascular Disease. It was noted that the advice was based on the beneficial effect of fish consumption on cardioavscular disease (CVD); the n-3 polyunsaturated fatty acids (PUFA) present in fish, eicosapentaenoic (EPA) and docosahexaenoic acid (DHA), are thought to mediate the effect of fish consumption on CVD risk.

5. The FSA's advice to pregnant women, not to eat more than one portion of fresh tuna, or two medium sized tins, per week, was discussed. It was explained that the existing JECFA provisional tolerable weekly intake (PTWI) of 3.3 mg/kg bw/week for methylmercury in the general population was not considered sufficiently precautionary for pregnant women. The COT considered that the US-EPA reference dose of 0.1 mg/kg bw/day would be protective for pregnant women and breast feeding mothers.

Nutritional benefits

6. The nutritional evidence was considered. Two secondary prevention randomized controlled trials (RCT) showing a beneficial effect of fish consumption or fish oil supplementation on the incidence of CHD were discussed - the DART and GISSI trials. The dose of n-3 PUFA provided in both trials was about 0.8g/d, which is equivalent to between 2 and 3 portions of oily fish per week. The beneficial effect became apparent after three months supplementation and the mechanism underlying this was thought to be either an antithrombotic or antiarrhythmic effect of n-3 PUFA.

7. Higher doses of n-3 PUFA (greater than 1.5 g/d) have beneficial effects on CVD risk factors, e.g. lowering plasma triacylglycerol concentrations. In the secondary prevention RCT no effect on plasma triacylglycerol concentrations was observed. It was noted that ongoing trials are investigating whether n-3 PUFA have antiarrhythmic effects in humans, and these should conclude later in 2003; furthermore, a primary prevention RCT examining the effect of n-3 PUFA on CHD incidence was planned in Italy.

8. The levels of supplementation, therefore, used in both the secondary prevention RCT and those required to beneficially affect CVD risk factors were greater than the current recommendation levels. If dietary recommendations were based on the RCT data the recommendation would be for people to consume 2-3 portions of oily fish per week.

9. In some prospective epidemiological studies, in populations at relatively low risk of CVD, no effect of fish consumption on CVD risk was observed at the initial follow-up, however, a beneficial effect did become apparent with subsequent follow-ups. This suggests that fish consumption has effects over the long term. The effects observed in the secondary prevention RCT were short term and may, therefore, underestimate the effect of fish consumption over a longer period.

10. It was noted that is was difficult to extrapolate from the secondary prevention RCTs to the general population. And, that primary prevention trials would need to be very large and be conducted over a long duration, with subjects 'at risk' of CVD, and there might still be problems with applicability to the general population.

11. Several issues were raised: whether an antiarrhythmic effect of n-3 PUFA would be relevant to the general population; whether the mechanism by which fish consumption is observed to lower the incidence of CVD in prospective studies was known; whether life-time exposure was different to later exposure, as in the

secondary prevention RCT; and that long term studies with low doses were required.

12. The availability of n-3 PUFA from food sources other than fish was discussed. Alpha-linolenic acid (ALNA), the precursor fatty acid to EPA and DHA, is associated with a protective effect against CVD in prospective epidemiological studies; however, the metabolic effects of EPA and DHA are not replicated by ALNA when given at biologically equivalent doses (i.e. assuming an 8 to 1 conversion of ALNA to EPA). ALNA supplementation increased circulating levels of EPA, but not DHA. This raises the question of where DHA comes from in vegans and vegetarians during pregnancy: DHA is required for the neural development of the fetus.

13. The possible effects of n-3 PUFA consumption of fetal and neonate neurodevelopment were discussed. Some studies suggest a beneficial effect of n-3 PUFA consumption on neonate neurodevelopment, particularly for preterm infants.

14. Fish is also a rich source of selenium. Selenium intakes have reduced in the UK in the last couple of decades to about half the RNI value.

15. It has been suggested that metabolism of n-3 PUFA may be affected by consumption of n-6 PUFA, i.e. the dietary n-6:n-3 PUFA ratio may affect conversion of ALNA to its long chain derivatives. It was agreed, however, that there is little evidence to support this hypothesis.

Toxicological considerations

16. The toxicological evidence and contaminant levels were considered. It was noted that COT were unable to describe the consequences of regularly exceeding the dioxin and dioxin-like PCB TDI. This was due to insufficient evidence to identify a duration and degree of exceedance at which adverse effects occur. However short term variation in intake does not significantly alter the body burden and occasional exceedance of the TDI would not be expected to result in harmful effects, provided that intake averaged over a prolonged period is within the TDI. There has been a

continuing drop in dioxin and dioxin-like PCB intakes: greater than 75% reduction since 1982. This was due to reduced contamination of the environment with these compounds and their breakdown.

17. Exposure data demonstrated decreasing levels of dioxin and dioxin-like PCBs in human breast milk, which is indicative of the body burden; however, levels in adipose tissue were not known.

18. It was noted that the toxicological implications of brominated flame retardants (BFR) are being assessed by COT, and although there were vast uncertainties in the data, these compounds should not be excluded from consideration.

19. In June 2003 JECFA revised its PTWI on methyl mercury. A recent follow-up of the Seychelles Child Development Study, which correlated methyl mercury concentrations in maternal hair at the end of pregnancy with cognitive performance of their 9 year old children, was considered. In light of this update COT will revisit mercury contamination of fish. It was noted that the revised JECFA PTWI of 1.6 mμ/kg bw/week was considered protective of the entire population.

Discussion

20. General points were considered. It was observed that a substantial proportion of the UK population does not eat fish at all, and getting the population to achieve dietary recommendations was an issue.

21. SACN should reconsider the recommendation to eat fish as the evidence supporting this had strengthened since 1994 when COMA considered this issue. SACN should also consider the evidence for an effect of n-3 PUFA on neurodevelopment.

22. It was suggested that there should be a move to providing advice to an optimal intake of fish that reflected different population sub-groups, e.g. high-risk individuals

both with respect to CVD and exposure to toxic contaminants of fish.

23. Sustainability of fish stocks is a factor, and vegetable sources of ALNA were originally considered in this light, i.e. whether ALNA could had the same effect as EPA and DHA. Other sources of EPA and DHA include eggs, algal oils and possibly genetically modified plants.

24. With regard to the toxicological issues, the safety guidelines for both dioxins and methyl mercury were based on critical effects following fetal exposure associated with the accumulated maternal body burden. Therefore females up to the age of reproduction should be considered a high-risk group. It would be appropriate, therefore, to recommend a safe upper limit of fish consumption for this group. The COMA recommendation to eat 'at least' two portions of fish per week should be considered in light of this.

25. It would be important for SACN to have a detailed exploration of n-3 PUFA and their effects. There were a broader range of considerations, not just fish.

26. Fish oil supplements were discussed. It was noted that levels of mercury were low. Levels of dioxins had generally fallen and there were maximum allowed levels for dioxins, but not dioxin-like PCBs. It was likely that maximum allowed levels for dioxin-like PCBs would be set in 2004.

27. The FSA advises pregnant women not to take cod liver oil as this is high in vitamin A.

28. The issue of the mobilization of fat depots during pregnancy, lactation and weight loss and subsequent release of fat soluble components (e.g. dioxins) was discussed. It was noted that fat depots are in a constant state of flux, with specific compounds being mobilized.

29. It was agreed that in principle people need to be encouraged to eat more fish from an early stage of life, however, this needs to be reconciled with the toxicological data.

Future work

30. It was agreed that:

• COT will reconsider methyl mercury in light of JECFA's revised PTWI for methylmercury.

• SACN will consider advice on fish and n-3 PUFA, especially with regard to the early stages of life and neurodevelopment.

31. Once SACN and COT have considered their respective issues the inter committee will meet again.