

Scientific Advisory Committee on Nutrition

**Paper for discussion: Risk Analysis; SACN's approach
to Risk Assessment in Nutrition
Agenda Item 4**

Please see attached paper for consideration. The following annexes are also attached:

Annex

1. Risk Assessment in Practice.
2. Freudenheim J L. Study design and hypothesis testing: issues in the evaluation of evidence from research in nutritional epidemiology. *Am J Clin Nutr* 1999;69(suppl):1315S-21S.
And
Byers T, Lyle B and Workshop Participants. Summary Statement. *Am J Clin Nutr* 1999;69(suppl):1365S-7S.
3. Marshall J R, Chen Z. Diet and health risk: risk patterns and disease-specific associations. *Am J Clin Nutr* 1999;69(suppl):1351S-6S.

Please also see:

1. Office of Science and Technology. Review of Risk Procedures used by the Government's Advisory Committees Dealing with Food Safety. Sir Robert May, Professor Liam Donaldson and Sir John Krebs. DTI. July 2000
2. Department of Health. Folic Acid and the Prevention of Disease. Report on Health and Social Subjects No 50. London: HMSO 2000. (Available on request).
3. Department of Health. Nutritional Aspects of the Development of Cancer. Report on Health and Social Subjects No 48. London: HMSO 1998. (Available on request).
4. Brussaard JH, van den berg H, Hermus RJJ, Walter P. Approach of the US Food and Nutrition Board to daily nutrient requirements: 'A useful basis for

the European discussion on risk assessment of nutrients?'. Report on a Workshop organised by the European Academy of Nutritional Sciences (EANS) and TNO Food and Nutrition Research Institute, 11 December 1998, Brussels. *European J of Clinical Nutrition* (1999) 52, 786-791. (Sent by email).

5. Potischman N, Weed D L. Causal Criteria in Nutritional Epidemiology. *Am J Clin Nutr* 1999;69(suppl):1309S-14S. (Sent by email).
6. Byers T. The role of epidemiology in developing nutritional recommendations: past, present and future. *Am J Clin Nutr* 1999;69(suppl):1304S-8S. (Sent by email)
7. Truswell S A. Levels and kinds of evidence for public health nutrition. *The Lancet*, 7 April '01: Vol. 357;1061. (Available on request from the Secretariat).

Scientific Advisory Committee on Nutrition

Risk Analysis; SACN's Approach to Risk Assessment in Nutrition

PURPOSE

1. At the last meeting of SACN on 12/13 June the committee decided it should discuss and agree its role in the process of risk analysis, particularly a systematic process of risk assessment. This should include a discussion of the nature and quality of evidence available in public health nutrition, so that all members can reach a common understanding of the process of evaluating the evidence to formulate scientific advice.

INTRODUCTION

2. The process of risk analysis is made up of three interconnected elements:

- **Risk assessment**
 - Hazard identification
 - Hazard characterisation
 - Exposure assessment
 - Risk characterisation
- **Risk management**
 - Action to be taken in response to a risk.
- **Risk communication**
 - Explanation of the risk and the action to be taken.

DISCUSSION

3. A review of the risk procedures used by government advisory committees dealing with food safety was carried out in 2000 (OST, July 2000). The group was led by Sir Robert May (the Government's Chief Scientific Advisor), and included Professor Liam Donaldson (Chief Medical Officer) and Sir John Krebs (Chairman of the Food Standards Agency). The group assessed how different expert committees approached risk assessment, how information

about risk is communicated and the role of each committee in risk management.

Risk Assessment

4. The finding of the May Review was that risk assessment practice varied, with some committees using formally structured assessments, and others relying on expert judgement. The Group **believed that a systematic risk assessment is the best way of approaching risk.** What is required is a transparent structure to examine, display and debate the nature of the risk particularly when little is known about the risk being assessed. This is a key role for expert advisory committees.

Risk Communication

5. There should be a presumption at every stage towards openness in explaining the interpretation of scientific advice. The aim should be to publish widely the scientific advice and all relevant papers, so that those outside can satisfy themselves about the process by which advice is formulated, and that conclusions have been correctly drawn.
6. In presenting advice to the public, it is important to give scientists a leading role in explaining their advice on science. Committees should operate in an accessible manner, seeking views widely, making available their considerations of evidence and explaining the reasons for their conclusions. Departments also have a duty to describe how policies have been formulated in response to the advice.

Risk management

7. Once the best information is available on the type and magnitude of risk Departments must decide on the action that should be taken. This is a matter reserved for them although expert advisory committees may be asked to comment on the available options.

ROLE OF SACN

8. It is one of the guiding principles of the FSA that our assessments of food standards and food safety "...will be unbiased and based on the best available scientific advice, provided by experts invited in their own right to give independent advice."
9. SACN has a role in risk analysis through its terms of reference, which state that it exists to advise the CMOs and/or FSA, and thus the Government on scientific aspects of nutrition and health. **Its risk assessments** should be systematic and evidence based along the lines considered by the May review, taking in a wide variety of evidence and subjecting it to scrutiny.

Through openness and transparency of its processes, reports, and open meetings SACN will contribute to **risk communication**.

10. Risk assessment in matters of diet, nutrition and health involves amongst other things making epidemiological comparisons between populations with chronic exposure to a certain dietary pattern and those who have not been exposed or with those who have managed the risk from exposure successfully. Such comparisons together with critical evaluation of scientific evidence lead to advice and help to formulate policy on risk management. In assessing risk posed by diet, particularly with regard to multifactorial diseases such as heart disease and cancer, the usual practice has been to assess relative risk which does not indicate the actual proportion of risk that can be attributed to nutritional factors. Assessment of absolute risk from nutritional/dietary factors to public health should be considered in order to enable effective risk management.
11. Further information on approaches to risk assessment in nutrition is attached at Annexes 1, 2 & 3.

CONCLUSION

12. Risk analysis is a key concept in developing evidence-based policy to achieve significant positive outcomes in the field of nutrition. A structured approach to risk analysis has been developed by government and SACN will have a significant role in delivering quality risk assessment and risk communication.

Members are invited to:

1. Note and comment upon the proposals for their role in the process of risk analysis;
2. Discuss their general approach to the evaluation of evidence which they may use in their deliberations in relation to public health nutrition;
3. Agree to make transparent at the beginning of any aspect of the work programme how they plan to structure their approach to the evidence available for a particular subject. This may vary depending on the subject.

**SACN Secretariat
September 2001**

ANNEX 1

RISK ASSESSMENT IN PRACTICE

This section address the following points:

- Examples of risk assessment in public health nutrition,
- levels and examples of evidence for public health nutrition and
- causal criteria, in order to form the basis for a discussion on SACN's approach to risk assessment.

a) Examples of risk assessment in public health nutrition

Folic Acid

1. An example of an approach to risk in public health nutrition arises in the COMA report on Folic Acid and the Prevention of Disease (DH 2000). The proven benefit of folic acid supplementation in a small group of women in the prevention of neural tube defects in their offspring must be set against potential adverse effects of folic acid where there is concurrent Vitamin B₁₂ deficiency which generally occurs in older people. There is also some evidence that higher folate intakes may benefit the entire population in terms of preventing cardiovascular disease and mental deterioration such as Alzheimer's. However, the hazards and benefits are very difficult to assess, because of the uncertainty over much of the evidence. It is difficult to assess with accuracy the size of the benefits and hazards to different groups. Adverse effects associated with nutrition may take decades to show, or be associated with genetic polymorphisms which are as yet uncharacterised. The analysis of risk in relation to folate/folic acid therefore took into account:
 - Adverse effects of inadequate folate on haemopoiesis (formation of blood cells) and on mucous membranes (e.g. lining of mouth) for over 50 years
 - Recently identified risk of neural tube defect (e.g. spina bifida)
 - Evaluation of available data on the risk of adverse effects from excessive intakes especially when given as folic acid supplements, which is synthetic and more bioavailable than natural folate in foods
2. COMA were reassured that there had not been increasing numbers of reports of adverse effects from increasing intakes of folic acid from fortified foods and increasing use of supplements in the US, but also recognised that the monitoring of adverse effects may well not be sufficient or comprehensive. Therefore, some judgement contributed to the risk assessment.

Diet and Cancer

3. The Working Group on Diet and Cancer of COMA had the remit to advise on the relationship between nutrition and the development of cancer and to make recommendations. The Committee noted in their report that there are

recognised principles for evaluating whether an observed association between an exposure and disease is likely to be causal, that it is more difficult to conclude that there is evidence for a lack of causality than for a causal relationship. The Group drew upon criteria developed by the International Agency for Research on Cancer (IARC) into five categories from being 'definitely carcinogenic to humans' through to 'probably not carcinogenic to humans'. In many cases, the data being applied were imperfect, and again, some conclusions were based on judgements based on rigorous interrogation of the data available. Relative risks of cancers attributed to intakes of particular foods were generally found to be small in relation to the risks from carcinogens in cigarettes or some occupational carcinogens. However, as diet is related to some very common cancers, small changes in relative risk might have larger effects on the population as a whole.

b) Levels and kinds of evidence for Public Health Nutrition

4. Nutritional epidemiology addresses the question of what factors lead to disease in human populations (Freudenheim 1999). These studies must take into account non-dietary factors as well in order to disentangle those dietary factors which are most important, and the strengths of the associations. Further information about epidemiological study design and the role of nutritional epidemiology is provided in **Annex 2**.
5. Evidence based advice is needed to develop dietary guidelines for the population. It might also be used to validate health claims (Truswell 2001). Depending on the type of advice being given, the committee may decide on levels of scientific evidence or the weight it will attach to different types of evidence. An example of this might be the Australia/New Zealand Food Authorities' levels of evidence, which are used to provide a guide for assessing the relationship between diet and disease (Truswell 2001):
 - Grade A: Systematic review of all randomised controlled trials (RCTs)
 - Grade B: Properly designed RCTs or well designed pseudo-randomised RCTs
 - Grade C: Cohort studies
 - Grade D: Case-control studies or interrupted time-series with a control group
 - Grade E: Comparative studies with a historical control
 - Grade F: Case-series
 - Grade G: Other relevant information, such as reports of expert committees
6. The important point which must be made, particularly in relation to assessing the interaction between diet and disease is that rank order should not be the only basis upon which to assess the value of evidence. Randomised controlled

studies may be seen as a potential 'gold standard' in some fields such as drug development. However, if the study is too small or the results have not been repeatable then the evidence is not strong. Cohort studies using well validated dietary assessments, with corrections for confounders, and which confirm the findings of other similar studies in different populations may be more useful.

7. Controlled trials looking at the 'whole diet' are highly complex, labour intensive and expensive and are therefore rare. Intermediate outcomes are often used because influences on outcomes such as death or late disease take decades to observe. Examples of intermediate markers are blood pressure, or plasma cholesterol. Therefore, conclusions may be drawn in two steps: for example, meta-analysis of controlled trials show that dietary saturated fats increase cholesterol. Cohort studies find that plasma cholesterol is an independent risk factor for cardiovascular disease. Thus, the conclusion is that saturated fat in the diet increases the risk of cardiovascular disease (Truswell 2001). A similar argument is used for sodium (salt) in the diet in relation to blood pressure and risk from stroke.

Factors which may guide deliberations

8. In the Report of the COMA Working Group on Diet and Cancer, the following factors were taken into consideration:
 - The type of epidemiological study – prospective studies carried more weight than case-control or ecological
 - Consistency of results between studies – both of same and different design and between those conducted in different circumstances
 - The quality of studies reviewed - more emphasis on those of better quality and design
 - A general tendency for the results of all studies to be in the same direction – even if not statistically significant. However, the possibility of bias due to preference for publishing positive studies must be taken into account.
 - The size of relative risk
 - A graded response – although lack of graded response should not be ignored as there may be a threshold effect
 - Evidence of an effect from randomised controlled trials
 - The exposure shall precede the effect – i.e. a temporal (causal) relationship between exposure and effect.
 - Evidence for a plausible mechanism
9. Evidence from animal studies needs to be considered carefully as this may not be relevant to humans, but may give clues as to mechanisms for causality.
10. In the case of cancer, most of the evidence was insufficient to establish either a causal association or a lack of association. Judgements were applied to 'variously inadequate evidence'.

c) Causal Criteria

11. In summary, for the purpose of making nutrition recommendations, there are five criteria:
 - Consistency
 - Strength of association
 - Dose response
 - Biological plausibility
 - Temporality
12. The more strongly the evidence supports the criteria, the easier it is to make recommendations. Ethical considerations may also come into play. For example, any presumed harm should not be ignored in presence of strong evidence of benefit. (Potischaman and Weed, 1999).
13. Epidemiological concepts such as relative risk, dose response, and threshold effects, may also be the subject of debate (Marshall and Chen, 1999). For further discussion of these concepts please see **Annex 3**.

**SACN Secretariat
September 2001**

ANNEX 2

1. Freudenheim J L. Study design and hypothesis testing: issues in the evaluation of evidence from research in nutritional epidemiology. *Am J Clin Nutr* 1999;69(suppl):1315S-21S.
2. Byers T, Lyle B and Workshop Participants. Summary Statement. *Am J Clin Nutr* 1999;69(suppl):1365S-7S.

ANNEX 3

1. Marshall J R, Chen Z. Diet and health risk: risk patterns and disease-specific associations. *Am J Clin Nutr* 1999;69(suppl):1351S-6S.