



Paper for Agreement: A Framework for Evaluation of Evidence that Relates Food and Nutrients to Health

Agenda Item: 4

Members are requested to note the SACN working document that provides a framework to the evaluation of evidence that relates food and nutrients to health.

A Framework for Evaluation of Evidence that Relates Food and Nutrients to Health

This document has been prepared for use by SACN in evaluating evidence that relates food and nutrients to health. It is a working document and as such may be subject to amendment depending upon requirements and experience with its use.

Issues for consideration by SACN may originate from a variety of sources, often in response to emerging evidence. Requests may come from the sponsoring departments, or from special interest groups, industry or because of developments in legislation at EU or other international organisations. Views from other expert bodies, either UK or international may also precipitate discussion. At the outset it should be made clear as to how evidence will be considered and to what extent taking into account of the timeframe and available resources. The goals of a subgroup or working party can be clarified through their terms of reference.

A DEFINING THE ISSUES (Background to the evaluation)

Subject of the evaluation (may be Terms of Reference)

- Principal nutrients or foods under consideration
- Relevant health or disease endpoints of the evaluation
- Putative role of foods or nutrients in process (i.e. characterisation of the possible role of nutrition in this area)
- Reason for review being undertaken (i.e. new evidence; issues raised by or relating to consumers; request of ministers/other departments; request from industry; EU or international reasons).

Present state of knowledge

- Background/Current state of knowledge (reference previous DoH/FSA/international reports and reviews)
- Current public health policy on issue

B ASSESSMENT (i.e. Quantification of risk/benefit)

The approach to the literature should be described. If certain types of evidence are not to be considered (eg animal or cell studies), this should be noted giving reasons for non-inclusion.

- **It is important to consider aspects of the statistical methods used in all study types. In particular:**

1. Appropriateness of statistical methods
2. Confounding factors taken into account
3. Potential for meta-analysis
4. Consistency of meta-analysis results

- **The following factors should be addressed whatever the study type:**

Causal criteria:

- a) Consistency of association with the health issue under consideration
- b) Magnitude of the association
- c) Dose Response
- d) Biological plausibility
- e) Temporality

Confounders and effect modifiers:

- a) Gender effects
- b) Age (infancy, childhood, adolescence)
- c) Ethnicity
- d) Pregnancy and lactation
- e) Smoking and other lifestyle and environmental factors
- f) Genotype
- g) Other lifestyle factors, eg physical activity, smoking

- **The following types of studies may need to be considered taking account of relevant factors for each type of study:**

Epidemiology and Randomised Controlled Trials

- a) Studies tabulated, including date, location, number of subjects and main results (ecological studies may not have to be listed individually.)
- b) Dietary methodology used and its validity
- c) Biomarkers of dietary exposure used and their validity
- d) Sampling and/or method of randomisation
- e) Drop out rate or loss to follow up (attrition)
- f) Data analysed according to validation of exposure assessment and health outcome
- g) Influence of common polymorphisms in functionally relevant genes
- h) Conclusions from studies

Human physiological studies

- a) Studies tabulated, including date, location, number of subjects and main results.
- b) Selection of subjects (age, ethnicity etc)
- c) Duration of studies (short term/long term)

- d) Biomarkers of dietary exposure used and their validity
- e) Success of intervention in achieving dietary intake
- f) Components of diet that have changed i.e. energy, macro and micronutrients, amounts etc
- g) Nature and appropriateness of study design: parallel, sequential or crossover, whether randomised
- h) Markers of compliance measured (blood, urine etc)
- i) Drop out rate
- j) Association of endpoint with health outcome
- k) Influence of common polymorphisms in functionally relevant genes
- l) Conclusion from studies

Clinical studies.

- a) Number of subjects and dates of studies tabulated
- b) Selection of subjects (age, ethnicity etc)
- c) Duration of studies (short term/long term)
- d) Principal clinical conditions studied. Validity of models used appertaining to the issue
- e) Biomarkers of dietary exposure used and their validity
- f) Success of intervention in achieving dietary intake (compliance)
- g) Components of diet that have changed i.e. energy, macro and micronutrients, amounts etc
- h) Nature and appropriateness of study design: parallel, sequential or crossover, whether randomised
- i) Markers of compliance measured (blood, urine etc)
- j) Drop out rate
- k) Association of endpoint with health outcome
- l) Influence of common polymorphisms in functionally relevant genes
- m) Drug usage taken into account
- n) Conclusion from studies

Sociological/Psychological studies

All of the above listed criteria may or may not be relevant particularly in the case of qualitative research and the approach to evaluating such research should be modified as appropriate. The following questions may be asked of the research¹.

- is work was relevant to the question,
- is the research question/s clear
- is the design of the study appropriate to the question
- is the context adequately described so that the reader can relate the findings to other settings
- does the sampling include a full range of possible cases/settings, have efforts been made to obtain data that might contradict or modify the analysis by extending the sample

¹ Criteria adapted from 'Qualitative Research in Health Care', Catherine Pope and Nicholas Mays, 2nd Edition, BMJ Books, 2000

- is the data collection and analysis procedure systematic, is there an audit trail, does the analysis include all the observations, are there unexplained variations, has the researcher developed concepts or categories to explain key processes/respondents' accounts or observations, is it possible to follow iteration between data and explanations given for the data, does the researcher seek cases which disconfirm
- does researcher assess impact of method on data, are enough data included in the report

Animal studies:

- a) Studies tabulated, including date, location, species, sex, number of animals, main results.
- b) Grounds for selection of studies
- c) Extent to which data from animal studies likely to be relevant
- d) Consistency of data and the extent of impact of diet
- e) Suitability of animal model (anatomy/metabolism/pathophysiology) for the particular diet-disease relationship of interest
- f) Comparability of dietary exposures to human dietary intake levels (in UK/Europe)
- g) Components of diet that have been altered eg energy
- h) Consistency of age/stage of growth of the animal with the age of appearance of the disease in humans
- i) Conclusion from studies

Cellular and molecular studies

- a) Number of subjects/samples and dates of studies tabulated
- b) Extent of cellular/ molecular basis of the disease
- c) Evidence for direct effects of nutrient or their metabolites on cellular processes (e.g. cell signalling mechanisms, transcription factors, gene and protein expression, cell proliferation, differentiation, apoptosis)
- d) Extent to which data from cell studies likely to be relevant
- e) Appropriateness of cell models to the human tissue(s) of interest e.g. possessing functionally relevant genes and proteins
- f) Use of physiological levels of nutrients, metabolites or nutrient sensitive endocrine exposures in cell studies
- g) Influence of common polymorphisms in functionally relevant genes
- h) Conclusion from studies

C KEY FACTORS TO ADDRESS WHILE DRAWING CONCLUSIONS

- Strengthen the available evidence to allow firm conclusions to be drawn and to be the basis for advice
- Principal areas of uncertainty
- Areas of further research required
- Significance of other lifestyle factors (exercise, smoking, stress etc) in contributing to issue. Extent to which dietary modification contributes to the problem.
- Can the risks or benefits be quantified?
- Advice based on all available evidence (Committee may flag up issues/views that are relevant to the consideration and implementation of any risk management)

Some general points for guidance when drafting findings or advice:

- The methods used for the review should be described - including details of data sources, databases searched and search strategies. Preference should be for data published in peer-reviewed journals, but other sources such as official or expert reports, official statistics, government funded research, may provide some valuable information. Where such data are used, the source should be clear.
- The findings of the review and the basis of advice should be clearly and consistently described. Descriptors should allow ready assessment of study quality and the validity of findings.
- The main results should be tabulated or listed.
- Basic statistical information needs to be included so that the strength of findings can be seen (at least the number of cases included in the analysis and the 95% confidence interval).
- Markers of study quality should be highlighted, including power, validity of biomarkers, participation rate (for cases and controls), attrition and whether or not confounding has been considered, appropriateness of statistical analysis, appropriateness of measures of dietary exposure or health outcome,.
- It may sometimes help clarity if results are presented graphically. Interpretation may be improved by indicating the amount of statistical information provided by a study as proportional to the size of the point plotted (e.g. area of a square). More informative studies then have larger points that make a stronger visual impression, counteracting the tendency for the wide confidence intervals on the estimates from small studies to draw the eye of the reader.

- There are a number of ways in which studies could be grouped for presentation. Grouping could be done according to study design or other major factors that may influence the results.
- A useful guide to reviewing and presenting findings can be found at www.york.ac.uk/inst/crd/report4.htm

The safety assessment of novel foods is undertaken by the UK Competent Authority Advisory Committee on Novel Foods and Processes (ACNFP) and in the case of some foods includes nutritional assessment. Specific criteria for nutritional assessment of novel foods was recommended by COMA in 1993 (**Annex 1**). The relationship of ACNFP with other food related committees is given in **figure 1**.

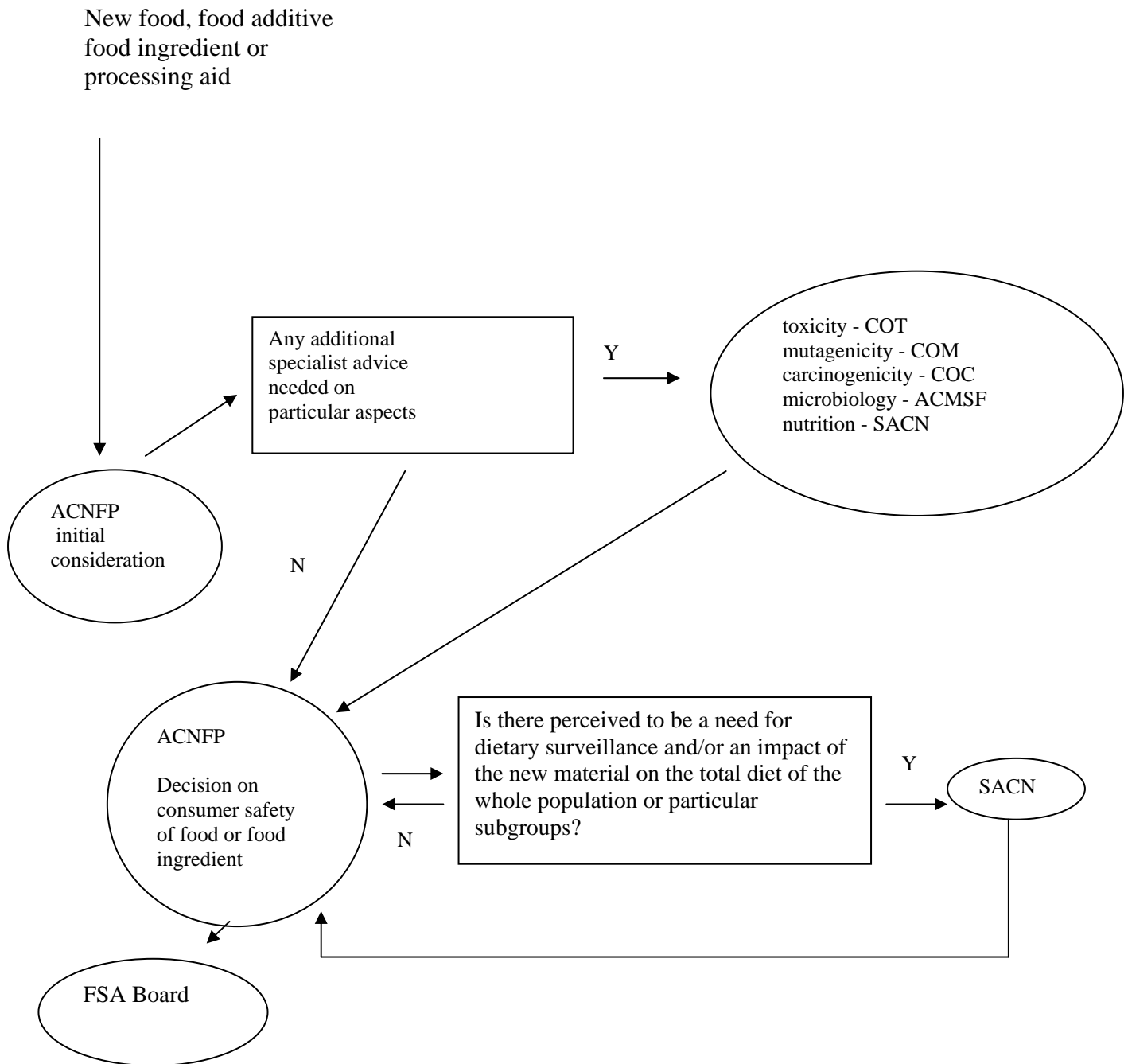
Annex 1**Nutritional Criteria for the Assessment of Novel Foods ²**

- a) The dietary significance of the novel food;
- b) The nutrient content of the diet as eaten containing the novel food, and the content of any anti-nutritional constituents (such as trypsin inhibitors) that may be introduced in to the diet with the novel food;
- c) The bioavailability of the nutrients in the novel food itself, the food's possible effects on other components of the diet, such as the mineral content, and any implications of possible changes that might be induced in the gut microflora;
- d) The effects of the novel food on the bioavailability of nutrients from other foods in the diet;
- e) The quantitative effects and/or dose response relationships of the novel food in relation to gut and systemic functions.

The relationship between the Advisory Committee on Novel Foods and Processes (ACNFP) and SACN is shown in **Figure 1**.

² The Nutritional Assessment of Novel Foods and Processes; Report of the Panel on Novel Foods of the Committee on Medical Aspects of Food Policy

Figure 1: Relationship of ACNFP with other expert committees involved in the assessment of food safety³



³ The Nutritional Assessment of Novel Foods and Processes; Report of the Panel on Novel Foods of the Committee on Medical Aspects of Food Policy

- Key:
 ACMSF – Advisory Committee on Microbiological Safety of Food
 ACNFP – Advisory Committee on Novel Foods and Processes
 COC – Committee on Carcinogenicity
 COM – Committee on Mutagenicity
 COT – Committee on Toxicity
 FSA – Food Standards Agency
 SACN – Scientific Advisory Committee on Nutrition