



**SACN framework for the
evaluation of evidence**



Scientific Advisory Committee on Nutrition

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

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Terms of reference

1. The Scientific Advisory Committee on Nutrition (SACN) is a UK-wide advisory committee set up to replace the Committee on Medical Aspects of Food and Nutrition Policy (COMA). It advises the UK Health Departments and is supported by a Department of Health Secretariat.
2. Its advice covers scientific aspects of nutrition and health with specific reference to:
 - Nutrient content of individual foods and advice on diet as a whole including the definition of a balanced diet, and the nutritional status of people;
 - Monitoring and surveillance of the above aspects;
 - Nutritional issues which affect wider public health policy issues including conditions where nutritional status is one of a number of risk factors (e.g. cardiovascular disease, cancer, osteoporosis, obesity);
 - Nutrition of vulnerable groups (e.g. infants, the elderly and ethnic minorities) and health inequality issues;
 - Research requirements for the above.
3. SACN's remit is to assess the risks and benefits of nutrients/dietary patterns, food or food components to health by evaluating scientific evidence and to make dietary recommendations for the UK based on their assessment. Conclusions drawn from any evidence considered are those that are applicable to the UK population, including any vulnerable groups which have been identified. Before providing advice, SACN assesses the possible risks that may be associated with implementing particular recommendations e.g. the potential risks of excess intakes or adverse impacts on other health outcomes or nutrients. In addition, principal residual areas of uncertainty are identified and form recommendations for further research. However, the committee does not advise on how recommendations are taken forwards for policy i.e. the committee's role is risk assessment and not risk management.
4. This document has been prepared for use by SACN in evaluating evidence that relates both food and nutrients to health. It is a working document that will be subject to regular review and may be amended depending upon the nature of the work.

Relationship with other committees

5. If SACN needs to assess evidence from other areas of science, appropriate expert advice will be sought e.g. from the Committee on Carcinogenicity, Committee on Mutagenicity and Committee on Toxicity. Conversely, if another scientific committee requires nutrition expertise a SACN representative will be co-opted onto that committee to provide the necessary advice. An example of this is the safety assessment of novel foods undertaken by the UK Competent Authority Advisory Committee on Novel Foods and Processes (ACNFP) which includes nutritional assessment. Specific criteria for nutritional assessment of novel foods were recommended by the Committee on Medical Aspects of Food Policy (COMA) in 1993. The relationship of ACNFP with other food related committees is illustrated in [Annex 2, Figure 1](#).

Defining the issues

6. To define the scope of the evaluation and identify specific questions SACN considers the following issues:
- Reason for review being undertaken (i.e. new evidence; request from Government Ministers, UK Health Departments, other Government departments; request from industry, or otherwise; developments from other expert bodies and changes in European legislation).
 - Principal nutrients, dietary patterns, foods and/or food components under consideration.
 - Relevant populations and health or disease outcomes of the evaluation. This decision is based on the published literature of health outcomes which are important to public health in the UK.
 - Putative role of nutrients, dietary patterns, foods and/or food components in establishing health or disease outcomes.
 - Background/current state of knowledge, including reference to previous UK Health Departments/Food Standards Agency/international reports (eg World Health Organization) and reviews including past SACN/Committee on the Medical

Aspects of Food Policy reports, devolved government reports, and/or good quality reviews from non-governmental organisations.

- Current public health policy on nutrition and health issue.

7. If conducting a full risk assessment, the above considerations can be used to inform the Terms of Reference of a SACN Subgroup or Working Group¹.

Reporting of evaluation

8. Once the issues have been defined, the format of the evaluation is chosen. SACN evaluations are reported in two main ways: risk assessments and position statements. A risk assessment involves looking at the totality of the evidence and assessing the potential risk and/or benefit of a particular nutrient/food/dietary pattern in terms of health. In evaluating evidence, uncertainties and inconsistencies in the evidence are highlighted and considered. Risk assessments provide advice to inform public health policy, identify future research needs and, when the evidence permits, may lead to public health recommendations on dietary intakes. Risk assessments are subject to public consultation, the responses of which are considered before the evaluation is finalised and published.
9. Position statements can take the form of a scoping exercise where a preliminary search of the evidence is performed to inform whether a risk assessment on a particular nutrient, dietary pattern, food or food component is required. They are not subject to public consultation and conducted when a formal risk assessment is deemed either not appropriate or not feasible. Position statements generally provide commentary on the nature of the evidence base for a particular nutritional issue and reach conclusions, but do not give public health recommendations. They can also be written in response to emerging issues which can arise from the UK or from international bodies e.g. European Food Safety Authority, World Health Organization.

¹ Both a Working Group and Subgroup consists of SACN members and external experts who are co-opted onto a Group when SACN requires additional specialist knowledge. Subgroups have a continuous work programme whereas a Working Group is formed on an ad hoc basis to address a particular issue resulting in a specific position statement or risk assessment.

Preliminary work

10. Prior to commencing the work, SACN sometimes scopes existing literature such as systematic reviews or expert committee reports to assess whether these can inform SACN's evaluation. In addition, a call for evidence may be published in order to identify relevant research in the field that is either ongoing, recently completed or due to be published to ensure contemporary evidence has not been overlooked.

Nature of evidence

11. When addressing a nutritional issue, all the evidence is considered at the outset and when drawing conclusions. Each Working Group or Subgroup specifies which study designs to include in their review. This varies depending on the question being asked and the evidence available.
12. Evidence can broadly be seen as either hypothesis testing or hypothesis generating. SACN is primarily concerned with making recommendations based on hypothesis testing evidence i.e. from studies that have been designed *a priori* to evaluate cause-effect relationships between a nutrient, dietary pattern, food/ food component and physiological outcomes in humans relevant to health/disease. In addition, supporting evidence is used to help explain how an exposure could be linked to the outcome to provide biological plausibility from mechanistic studies in humans, animals, tissues or cells. In the process of producing research recommendations SACN may also identify potential nutritional hypotheses to be addressed.

13. Historically a ‘hierarchy of evidence’ has been used as a framework against which to judge the strength of evidence according to study design. This is because different study designs have different strengths and weaknesses and, therefore, value in informing decisions. Typically, most weight is given to good quality randomised controlled trials (RCTs) with less weight given to observational (non-intervention) studies. This is because observational studies are potentially subject to bias, confounding and reverse causality. Guidance provided by the NHS Centre for Reviews and Dissemination (CRD) provides an example of this approach and also includes a list of study definitions.²
14. However, it is not always appropriate to conduct RCTs due to feasibility or ethical considerations or this form of evidence may simply not be available, consequently there may be few trials to draw on. In the absence of RCTs, evidence from well conducted quasi-experimental³ and prospective studies is considered stronger evidence than other study designs. Well conducted high quality systematic reviews may also be used to inform SACN’s deliberations. The purpose of conducting a systematic review is to capture all the available literature to answer a specific research question according to a pre-defined process and criteria. As with all study designs, RCTs, systematic reviews and observational studies are only as good as the methods employed, and their value in informing recommendations is dependent on study quality. SACN bases its public health recommendations on the best quality of evidence available.
15. Judgement on whether a particular nutrient, dietary pattern, food and/or food component is contributing to any observed effects in the outcome are based on the quality and quantity of the available evidence. This is of particular importance when reaching conclusions following a risk assessment.

² Systematic Reviews: CRD’s guidance for undertaking reviews in healthcare, ISBN: 1900640473.

³ Quasi-experimental studies are non-randomised intervention studies and include a range of study types such as non-randomised controlled studies, before and after studies and interrupted time series. See the above CRD guidance for definitions of these specific study types.

Methodology

16. Before work commences each Working Group, Subgroup or Drafting group⁴ decides on the criteria for the selection of original research, which in turn informs how the evidence is to be reviewed. The rationale for the chosen review approach is made clear.
17. When conducting a comprehensive narrative review or a systematic review the methods used are described in detail. Details of data sources used, databases searched and particular search strategies are provided for both approaches. Preference is given to data published in peer-reviewed journals, but other sources such as official or expert reports based on peer-reviewed literature and official statistics may provide some valuable information. Where such data are used, the source is specified and accessible to others. Generally, SACN considers evidence up to an agreed cut-off date; however if studies published after this point are considered sufficiently important they will also be deliberated.
18. If certain types of evidence are not to be considered/included, this is noted and the specific reasons for non-inclusion stated.
19. Consideration is given to the:
 - Scope of review- exposures, outcomes, population, age range.
 - Search strategy e.g. databases to be searched, if hand searching is to be performed, other sources of information, search terms, study designs to include, publication date range.
 - Article type- published in peer reviewed journals, language.

⁴ A Drafting Group consists of approximately 3-5 SACN members who advise the Secretariat on drafting text on a particular issue or topic.

20. For systematic reviews, the methods are specified in full prior to beginning the review process. If SACN considers that a systematic review is required and feasible, it is performed according to established guidelines such as those from CRD or Cochrane Collaboration (see below). An expert in systematic review methodology may be co-opted onto Working Groups to advise on the systematic review process to ensure that reviews are conducted to a high standard.

The following guidance provides further details on systematic reviews:

Systematic reviews: CRD's guidance for undertaking reviews in healthcare-
Chapter 1

http://www.york.ac.uk/inst/crd/pdf/Systematic_Reviews.pdf

Cochrane Handbook for Systematic Reviews of Interventions

<http://www.cochrane-handbook.org/>

World Cancer Research Fund Systematic Literature Review Specification Manual

http://www.dietandcancerreport.org/?p=slr_specification_manual

Scottish Intercollegiate Guidelines Network (SIGN) Chapters 6 and 7

<http://www.sign.ac.uk/guidelines/fulltext/50/index.html>

Data Synthesis

21. The main results are tabulated indicating the author, date, country, sample size, duration of study, dietary assessment method, exposure, outcome, main results and adjustment for confounders. This list is not exhaustive and there maybe additional information which the committee may consider useful to include e.g. source of funding. Examples of data presented in SACN reports are given in [Annex 2](#).
22. Basic statistical information is captured so that the strength of findings can be identified.

Data analysis

23. When deliberating whether data analysis can be conducted from information extracted from the studies reviewed, the following issues are considered:

- Potential for meta-analysis
- When meta-analysis would be considered appropriate
- The models to be used and rationale e.g. random vs. fixed effect
- Consistency of meta-analysis results
- How heterogeneity will be assessed e.g. I^2 statistic and associated criteria.
- Investigation of publication bias
-

24. It may be helpful to present the results graphically e.g. forest plots.

Quality assessment of studies

25. SACN considers methodologies of the studies reviewed in order to assess their quality and this will influence the conclusions that can be drawn; examples of the factors that need to be considered during quality assessment are given in [Annex 1](#).

Key factors to address while drawing conclusions

26. When drawing conclusions on whether a causal relationship exists, the following considerations are included⁵:

- a) Type of study reviewed and its quality.
- b) Is there confidence that the observed effects are not due to confounding? What is the significance of other lifestyle factors (physical activity levels, smoking, environment) in contributing to the specified issue and the extent to which dietary modification contributes to the problem or may obscure relationships? Have appropriate adjustments been made for such known confounders?

⁵ Howick J, Glasziou P, Aronson JK. The evolution of evidence hierarchies: what can Bradford Hill's 'guidelines for causation' contribute? J R Soc Med. 2009 May;102(5):186-94

- c) Magnitude of the association- a large relative risk with a small confidence interval indicates that the effect may be causal. However, a small relative risk does not mean that an association does not exist.
- d) Power- is the study sufficiently powered to detect a difference, if one actually exists.
- e) Dose response- this is not an absolute requirement for causality because a threshold relationship may exist, but if apparent, a dose-response relationship provides additional evidence that the exposure is linked to the outcome.
- f) Temporality- the proposed cause (dietary exposure or lack of it) needs to precede the observed effect (health/disease outcome).
- g) Biological plausibility/mechanistic evidence- can the exposure be linked to the outcome and is it based on sound evidence consistent with known/accepted principles? Is there evidence to show that it is applicable to humans or reasons why it might not be?⁶
- h) Consistency of association with the health/disease outcome(s) under consideration- do other studies demonstrate similar findings either within the same study design or across different designs? Are the results in the same direction?

Public consultation

27. Once risk assessments have been completed, the initial report is put out to public consultation. The comments arising from this process are considered by SACN and, where appropriate, amendments are made before the final report is published. However, in some instances a public consultation on a particular issue is held before an assessment is undertaken e.g. a call for evidence (see section on [preliminary work](#)). Position statements are not subject to this process, however; all SACN advice is discussed at a committee meeting open to observation by the public before it is finalised.

COMA, Nutritional Aspects of the Development of Cancer, Department of Health, 1998

⁶ Howick J, Glasziou P, Aronson JK. Evidence-based mechanistic reasoning. J R Soc Med. 2010 Nov;103(11):433-41

Annex 1: Factors to address when assessing quality of studies

Statistics

28. It is important to consider aspects of the statistical methods used for all study types in the review, in particular:

- Statistical methods should be clearly described
- Appropriateness of statistical methods, particularly around the use of repeated measures analysis and handling of baseline values and covariates.
- Inclusion of detailed information on study power
- Whether confounding factors taken into account in the study design and subsequent analysis
- Reduction of systematic bias
- Distinction of *a priori* vs. *post hoc* hypothesis testing and reporting of associated results

Methodological considerations

29. There are certain methodological issues that need to be assessed when evaluating the evidence, some of which will be common to all study types and others are study specific. Important factors to address are listed below:

Randomised Controlled Trials

- a) Sample size/power
- b) Method of randomisation
- c) Blinding
- d) Selection of subjects (age, ethnicity etc.)
- e) Other inclusion and exclusion criteria
- f) Duration
- g) Nature and appropriateness of study design: parallel, sequential or cross-over (stated wash out period)
- h) Dose (physiological vs. pharmacological)

- i) Biomarkers of dietary exposure, nutritional status and/or intermediate health outcome used and their validity
- j) Appropriateness of control used
- k) Markers of compliance measured (blood, urine etc.)
- l) Success of intervention in achieving the required change in diet or nutritional status i.e. compliance
- m) Components of diet that have changed i.e. energy, macro and micronutrients, amounts etc. and how change in one component has influenced other elements of the diet
- n) Drop out rate or loss to follow-up (attrition)
- o) Relationship of endpoint measured with health/disease outcome(s) under consideration
- p) Baseline nutrition status
- q) Other *a priori* hypothesized sources of variance including polymorphisms in functionally relevant genes

Prospective cohort studies

- a) Sample size/power
- b) Method of drawing sample
- c) Method of recruiting participants
- d) Response to recruitment
- e) Length of follow up
- f) Dietary methodology used and the reported validity and reproducibility of that method
- g) Biomarkers of dietary exposure, nutritional status and/or intermediate health outcome used and their validity and comparability
- h) Drop out rate or loss to follow up (attrition)
- i) Components of diet that have changed i.e. energy, macro and micronutrients, amounts etc and how change in one component has influenced other elements of the diet
- j) Outcome assessment method used and whether this is self reported, measured or clinically assessed – and if intermediate the strength of its relationship to health outcome

- k) Data analysed according to validation of exposure assessment
- l) Baseline nutrition status
- m) Other *a priori* and *post-hoc* considered sources of variance including polymorphisms in functionally relevant genes

Social Science

30. Social science can be quantitative or qualitative and draws on a range of academic disciplines including sociology, psychology and anthropology. It is most often used to explore a topic in depth, collect information on perceptions, knowledge and behaviours and to evaluate policies and interventions. In addition to the considerations already discussed above, the following questions may also be asked of the research:

Study purpose/scoping

- Are the research objectives clearly defined?
- Is reference made to previous research and theory?

Design and sampling

- Is the research design (including sampling) discussed adequately and appropriate to address the research questions?
- Is the research design justified with any limitations discussed?

Data collection and ethics

- Were the data collected appropriately?
- Have ethical issues been considered and addressed?

Analysis

- Is the approach to analysis described? Is it systematic and appropriate?
- Does the data support any subgroup analysis carried out?
- Is the scope for drawing wider inference discussed?

Reporting

- Are conclusions supported by evidence?
- Does the summary accurately reflect findings?

- Is there any discussion on whether the findings support or contradict existing research?
- Has the study been peer reviewed and any concerns addressed?

The following provide further guidance:

Quality in Qualitative Evaluation: a framework for assessing research evidence

A Cabinet Office commissioned methodological review of quality standards in qualitative evaluation methods.

http://www.civilservice.gov.uk/Assets/a_quality_framework_tcm6-7314.pdf

10 Questions Framework

A framework of ten questions developed by Glasgow University to appraise the quality of studies that use a qualitative methodology

http://www.civilservice.gov.uk/Assets/Qualitative%20Appraisal%20Tool_tcm6-7385.pdf

Code of Practice for Official Statistics

<http://www.statisticsauthority.gov.uk/assessment/code-of-practice/index.html>

Animal and cellular/molecular studies

31. If animal or *in vitro* studies are to be evaluated, the following issues need to be considered:

Animal studies:

- a) Reasons for selection of studies
- b) Extent to which data from animal studies are likely to be relevant to humans
- c) Statistical power of the study
- d) Consistency of data and the extent of impact of micronutrients, macronutrients and whole diet

- e) Suitability of animal model (anatomy/metabolism/pathophysiology) for the particular diet-disease relationship of interest
- f) Comparability of micronutrients, macronutrients and whole diet exposures to human dietary intake levels (in UK/Europe)
- g) Components of diet that have been altered eg energy, macro and micronutrient intake
- h) Consistency of age/stage of growth of the animal with the age of appearance of the disease in humans

In vitro, ex vivo and molecular studies

- a) 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)
- b) Extent to which in vitro or ex vivo data are likely to be relevant to humans
- c) Appropriateness of models to the human tissue(s) of interest e.g. possessing functionally relevant genes, receptors and proteins
- d) Use of physiological levels of nutrients, metabolites or nutrient sensitive endocrine exposures in cell studies, taking appropriate account of bioavailability and bioaccessibility
- e) Influence of polymorphisms in functionally relevant genes
- f) Appropriate statistical analysis and control for multiple outcome measures (eg in '-omics' studies)

Annex 2: SACN tables

An example of data extracted from RCTs taken from the SACN Iron and Health report 2010.

Table A8: Short-term treatment trials in children aged ≤ 3 years with iron deficiency anaemia or iron deficiency

Study/year/ country	Sample	Age (months)	Study design and treatment	Exclusions	Outcome measures	Dropout	Findings	Remarks
Oski and Honig, 1978 USA	IDA (n=24) IDA treated IDA (n=12) IDA untreated (n=12) (IDA=Hb<105 g/L, MCV<74 serum Fe<15 µg/L, TS<13%)	9–26	DBRCT Treatment = IM Fe Placebo = IM saline Fe dose = enough to raise Hb to 120 g/L Duration: 5–8 days	Intercurrent illness or chronic disease	BSID IBR		<u>Baseline:</u> No significant differences in MDI or PDI between groups. <u>Treatment:</u> Change in MDI or PDI scores not significantly different between groups. Fe-treated group significantly increased in MDI. No significant change in PDI of either group. Treated group improved more than controls in reactivity ($p < 0.05$), gross and fine motor ratings ($p < 0.01$); attention not significantly different.	Small groups.

An example of data extracted from prospective cohort studies taken from the SACN Iron and Health report 2010.

Table A14. Total dietary iron and colorectal cancer risk

<i>Study/year/country</i>	Age baseline (y)	Mean Follow-up	Cases	Non-cases	Cancer site	Comparison (median intake or quantile range)	Adjustments	RR (95% CI)
Wurzelmann et al, 1996 USA	25-74	15	52 M+F	8,740 M+F	Proximal colon	Top fourth vs bottom fourth (intakes in quartiles not specified)	Age, sex	1.44 (1.23-1.69) p trend not given
As above	As above	As above	57 M+F	As above	Distal colon	As above	As above	1.03 (0.80-1.32) p trend not given
Kato et al, 1999 USA	34-65	4.7	105 F	523 F	Colorectum	Top fourth vs bottom fourth (intakes in quartiles not specified)	Age, beer intake, physical activity, family history CRC	1.17 (0.6-2.3) p trend=0.44

Annex 3: Nutritional Criteria for the Assessment of Novel Foods

Novel food applications

32. Under the 'Novel Foods Regulation' (Regulation (EC) No 258/97), a novel food is defined as a food that does not have a significant history of consumption within the European Union (EU) before 15 May 1997. Such foods are subject to a pre-market safety assessment before a decision is made on EU-wide authorisation. A novel food application is first made to a single EU Member State (see Figure). Once this application has been accepted the Member State has 90 days to produce an initial opinion. This opinion is then circulated to all EU Member States, who are then given a further 60 days to comment. In the UK, the Food Standards Agency is the Competent Authority, advised by the Advisory Committee on Novel Foods and Processes (ACNFP); a non-statutory, independent body of scientific experts. Assessments include a detailed study of potential for toxic, nutritional and allergic effects and ACNFP can call on the expertise of a range of committees in these areas (Figure 1), including the SACN. In addition, because of the importance of nutritional considerations, a nominated representative of SACN is also co-opted onto ACNFP. Guidelines on the assessment of novel foods and processes were published by ACNFP in 1991 and by COMA in 1993⁷.

⁷ Department of Health (1991) Guidelines on the Assessment of Novel Foods and Processes. Report on Health and Social Subject No. 38

Department of Health (1993) The Nutritional Assessment of Novel Foods and Processes. Report on Health and Social Subjects No. 44

Nutritional assessment

33. The Novel Foods Regulation states that foods or food ingredients falling within the scope of the regulation must not:
- present a danger for the consumer
 - mislead the consumer
 - differ from foods or food ingredients that they are intended to replace to such an extent that their normal consumption would be nutritionally disadvantageous for the consumer
34. The assessment is primarily based on the dossier submitted with the application. This includes data produced by the applicant, citation of relevant scientific publications and reports, and an assessment of the anticipated intake in the population. The last component is often critical to the nutritional safety assessment and usually specifies the anticipated maximum intake within the intended target group and the wider population, particularly children and other vulnerable groups. The nutritional assessment is concerned with factors such as the composition, the source organism and preparation method, nutritional benefit and/or safety, metabolism, intended use and the level of undesirable substances. Health claims are the responsibility of EFSA and are not considered. The nutritional assessment follows the SACN framework for the evaluation of evidence and includes an evaluation of the completeness and quality of the publications cited and whether the applicant's interpretation is reasonable. Current SACN/COMA/EFSA advice relevant to the novel ingredient or process is also considered. Should the SACN representative on ACNFP wish to take wider advice this may be referred to the SACN secretariat (consideration at full SACN open meetings may not be practical because of the statutory time limit on decisions and the inclusion of 'commercial restricted' information in the application). The SACN representative may be required to specify what additional data or information is required to carry out the assessment.

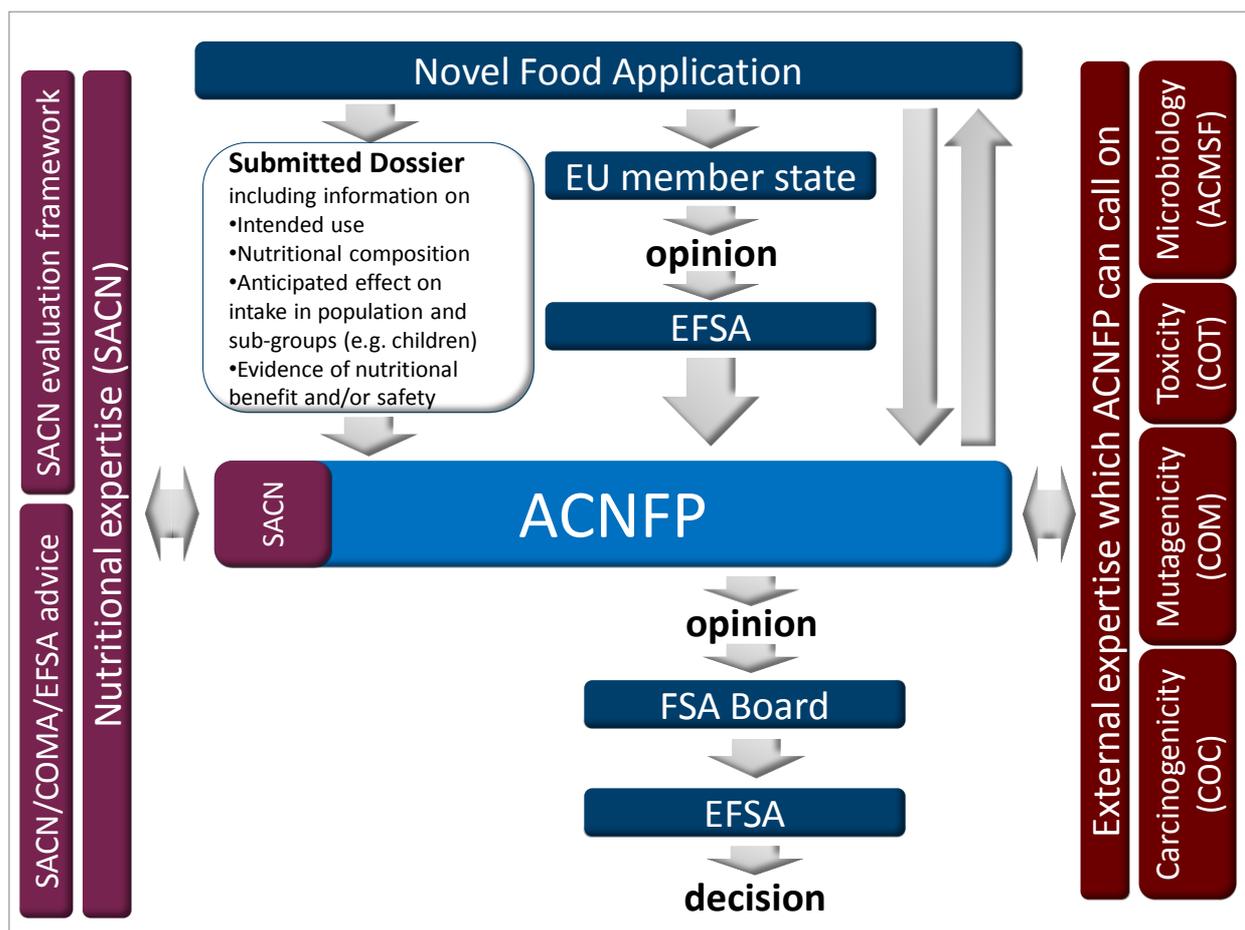


Figure 1- Relationship of ACNFP with other expert committees involved in the assessment of food safety.

Key

- ACMSF – Advisory Committee on Microbiological Safety of Food
- ACNFP – Advisory Committee on Novel Foods and Processes
- ANANF – Working group on Approaches to the Nutritional Assessment of Novel Foods
- COC – Committee on Carcinogenicity
- COM – Committee on Mutagenicity
- COMA - Committee on Medical Aspects of Food Policy
- COT – Committee on Toxicity
- EFSA - European Food Safety Authority
- EU – European Union
- FSA – Food Standards Agency
- SACN – Scientific Advisory Committee on Nutrition