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PASSCLAIM[1] – Report of the First Plenary Meeting including a set of interim criteria to scientifically substantiate claims on foods

Background

Whilst food provides us with energy and nutrients for growth and the maintenance of bodily function, it is becoming clear that, in the context of the lifestyle of people in developed countries, it can offer much more. Through its capacity to contribute to and control many metabolic, physiological and psychological functions of the body, food has effects beyond what is traditionally accepted as nutrition. Food can play an important role in reducing the risk of disease and, equally importantly for the healthy population, can help to optimise and enhance normal function and thereby improve quality of life. Out of this new concept of "optimal nutrition" and facilitated by significant advances in food science and technology has been born the idea of functional foods.

These new concepts have already stimulated health authorities, especially in Japan and the USA to support research on physiological effects and health benefits of food components. By 1991 in Japan and 1993 in the USA a system was in place to allow claims for food that could improve health or reduce disease risk. However, in the EU there is no harmonised legislation on health claims for foods, a situation that neither benefits the consumer nor helps the competitive position of the European food industry.

Against this background the EU agreed to fund in 1996 a concerted action entitled "Functional Food Science in Europe (FUFOSE)" with the aim "to develop and establish a science based approach for the emerging concepts in functional food development". FUFOSE, in its final consensus document (Brit J Nutr (1999) 81 Suppl 1) concluded that the development of functional foods must be based on sound scientific knowledge of the target function in the body and show that the effects are relevant to improved health or reduction of disease risk. It identified the development of "validated markers for these target functions and the evaluation of sound scientific data from human studies for their possible modulation by foods and food components" as an important part of the validation process. FUFOSE acknowledged that claims are an important means of communicating the benefit of functional food to the consumer. In 1997 Codex Alimentarius Commission had defined four forms of claims for food but FUFOSE felt these claims did not allow the benefits of functional foods to be communicated and proposed two additional ones:

- Type A: 'Enhanced function' claims
- Type B: 'Reduction of disease-risk' claims

In 1999 CODEX included these new claims in their definitions.

PASSCLAIM, an EU funded, ILSI Europe initiated concerted action, commenced in April 2001 and built on the principles arising out of FUFOSE.

In the first year of PASSCLAIM, four individual Theme Groups (ITG) were established with a view to critically assessing the evidence base for claims and the use and development of markers. The reports of these

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1 Process for the Assessment of Scientific Support for Claims on Foods

four groups, together with the FUFOSE Consensus Document, formed for the main background papers for the First Plenary Meeting, held in Berlin, Germany.

On the basis of the ITG reports, the steering committee of PASCLAIM drew up a "Draft set of interim criteria for the scientific substantiation of health claims on foods and food ingredients" (Table 1). These draft interim criteria were the starting point for discussions at the first Plenary Meeting and a revised set of Interim Criteria (see later) was the main output from the meeting.

Table 1 Draft set of interim criteria for the scientific substantiation of health claims on foods and food ingredients

SUBSET 1 "preconditions and hypotheses"
Precondition
1. Health claims should be considered within constraints of toxicological and nutritional safety. These are not part of the health claim, though, but can be part of the dossier supporting the claim.
Overall goals:
2. Health claims should be scientifically substantiated. The substantiation should be based on the totality of the available information.
3. Health claims should be made and assessed for the identified target population (A does B to C); the target population can be the population at large.
Tools:
4. The starting point for the substantiation of a health claim should be a review of generally accepted knowledge which generates a physiological or psychologically based hypothesis for the proposed claim and its substantiation.
5. The hypothesis should be based on a plausible mechanism or clear association and the physiological or psychological relevance should be valid.
SUBSET 2 "data"
6. Health claims should primarily be based on human intervention studies. Generic claims, however, do not require such studies with the food product. Observational epidemiological studies, animal model studies and *in vitro* studies form part of the supporting knowledge base for the hypothesis.
7. Human intervention studies should have a scientifically valid design compatible with the purpose of the study to show persistent effects, e. g.: a) Have sufficient statistical power to demonstrate the proposed benefit/or its surrogate outcome, b) Use study groups that are physiologically representative for the target consumer populations, c) Use appropriate controls, d) Have sufficient length, e) Demonstrate reproducibility of the study outcome.
8. Health claims should be based on a realistic/feasible amount of the food/food ingredients as consumed in the context of a total diet. A dose response relationship should ideally be demonstrated.
SUBSET 3 "markers"
9. Unless the endpoint itself can be measured, human intervention studies should use validated markers (markers of target function/biological response or intermediate endpoint).
10. The markers used should comply with the criteria for markers as laid down in the FUFOSE consensus paper (See appendix BJN 1999).
11. Upon intervention the marker should change in a statistically significant as well as physiologically or psychologically relevant way.

First Plenary Meeting

The meeting took place over three days in Berlin and was attended by around 80 delegates, approximately half of whom were from industry and the rest from academia or government. Twenty countries were represented including two candidate countries for EU membership in 2004, Hungary and the Czech Republic, three non EU countries, Israel, Turkey and Switzerland and there were representatives from ILSI Japan, USA and South East Asia. The meeting programme was arranged so that about 60 % of the time was spent in discussion either in plenary sessions or working groups.

The objectives of the First Plenary Meeting were:

1) To present the reports of the Individual Theme Groups (ITG)
   - Diet-related cardiovascular disease (A)
   - Bone health and osteoporosis (B)
   - Physical performance and fitness (C)
   - Review of the existing codes (D).
2) To evaluate the Draft Set of Interim Criteria.
3) To develop and agree a further set of Interim Criteria that will be tested by the ITGs on:
   - Insulin sensitivity and risk of diabetes (E)
   - Diet-related cancer (F)
   - Mental performance (G)
   - Gut health and immunity (H).

The first plenary session opened with brief remarks by the chairman of PASSCLAIM, Professor Nils Asp and by the session chair Dr Gérard Pascal. Dr Contor, Deputy Director of ILSI Europe, reminded the meeting participants that both FUFOSE and PASSCLAIM had been initiated by the ILSI Europe Functional Food Task Force, chaired by Dr Anne Franck. Dr Jürgen Lucas for the Commission DG Research updated delegates on progress in the 6th Framework Programme, Food Quality and Safety.

Professor Asp then outlined the background of PASSCLAIM, especially the role of FUFOSE. He emphasised that whilst FUFOSE had drawn a distinction between "Enhanced target function", leading to Type A claims, and "Reduced risk of diseases", leading to Type B claims, that in reality there was no clear boundary between these. He showed how FUFOSE had been important in providing input to the CODEX Alimentarius Commission's Committee on Food Labelling, for the Council of Europe Technical Document 2001, "Guidelines Concerning Scientific Substantiation of Health-related Claims for Functional Food" and for the European Commission in drafting its proposal for "Regulation of the Parliament and of the Council on Nutrition, Functional and Health Claims Made on Foods" (Working Document SANCO/1832/2002). He reiterated the aims of the First Plenary Meeting and urged delegates to focus on criteria for substantiation of claims.

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Diet-related cardiovascular disease (ITG A)

Professor Ronald Mensink, Chairman of ITG A, spoke to the group's report entitled "Diet-related cardiovascular disease". He said that the Group had reviewed those aetiological processes and risk markers of coronary heart disease, cerebrovascular disease and peripheral arterial disease that can be modified by diet namely lipid and lipoprotein metabolism, haemostatic function, oxidative damage, homocysteine metabolism and blood pressure. From an enormous wealth of publications in this, one of the most researched areas of food and health, the Group concluded that Type A claims (for enhanced function) could be made for diet-related changes in LDL and blood pressure. For HDL cholesterol, fasting triacylglycerol and plasma homocysteine biomarkers exist but it is as yet not clear if these biomarkers reflect, "enhanced function". For haemostatic function and oxidative damage, there is a need to develop validated biomarkers that are sensitive to dietary changes.

During the course of Professor Mensink's talk and in the ensuing discussion, the following additional points, which were also in the FUFOSE consensus conclusions, were emphasised.

- Cardiovascular diseases are multifactorial in their origins of which diet is one contributing environmental factor.
- Biomarkers denote "enhanced function" but ultimately it is health that is important. The relation of biomarkers to hard endpoints of morbidity and mortality need to be determined.
- Animal studies provide supportive but not conclusive evidence. Human studies are essential.
- Diabetes will be dealt with by ITG E. However, mention should be made of the importance of insulin sensitivity as a risk factor for atherosclerosis.
- The process of review should be formalised. An evidence-based approach should be used. This would provide a transparent and accountable process that would give more credibility to conclusions.
- Risk factors are inter-related. Integrating biomarkers together may be a more valid approach.

Bone health and osteoporosis (ITG B)

Dr Ann Prentice, Chairperson of ITG B, presented the Group's report, which was based on evidence drawn from a worldwide perspective, including that from third world countries. Although bone health problems encompass many skeletal disorders, the Group focussed on osteoporosis because this is a major public health issue in the EU. A framework was developed to describe the chain of evidence required to link consumption of a food or ingredient with bone health outcomes. Biomarkers of bone health were discussed and bone mineral density (BMD) was identified as the only marker that can, for people of any age and sex, provide evidence of enhanced function. For people over 50 living in countries with a high risk of fracture, BMD was considered to be marker of fracture risk such that changes in BMD caused by a food component could provide evidence of a potential reduction in risk. Claims will need to be made in the context of a healthy lifestyle.

Issues that emerged during the talk and subsequent discussion are as follows:

- There was still ambiguity about the definition of osteoporosis and controversy over whether low BMD is a risk factor or the disease itself. WHO has established a working definition based on BMD, whereas fracture is regarded as the clinically relevant outcome of the disease.
- Fracture risk can vary independently of BMD. For example, in some areas of China, BMD in older people is lower but risk of fractures is less than in Western countries. Similarly, sodium fluoride used therapeutically increases BMD but also can increase fracture risk. In addition, balance is an important predictor of fracture risk that is independent of BMD.
- Although peak bone mass is related to future fracture risk, it is not known whether increases in peak bone mass in young adults translate into alterations in later fracture risk.
- Claims that osteoporosis risk is reduced would in principle require clinical trials with fracture as an endpoint. However, such trials will be of very long duration and are likely to be impractical for a food company to undertake in relation to a claim. Further definition and substantiation of markers for change in fracture risk are therefore important.
- Claims that a food component reduces fracture risk or the risk of osteoporosis are likely to be regarded as a medicinal claim. The borderline between foods and pharmaceuticals, and the respective claims, needs to be clarified.

Physical performance and fitness (ITG C)

Professor Wim Saris, Chairman of ITG C, in presenting the Group's report reminded delegates that claims for food or ingredients enhancing performance had a long history. More than 150 claims had been identified. Claims were essentially Type A and were not usually linked to reduction of disease risk. The Group had reviewed claims relating to strength and power; endurance; energy supply and recovery; hydration status; flexibility; tissue growth and immune function. Many methods for measuring these parameters of fitness were examined as possible markers for claims. This included tests of muscle strength, energy metabolism, food intake, gastrointestinal function and immune function.

The Group had concluded that "for all physical performance and fitness domains, sets of biomarkers to substantiate claims are available" and that "for most areas, reliability and validity are good". The position was less clear for immune function.

In the subsequent discussion, the following points were made:

- Markers of fitness may also be valid markers of risk in other areas, e. g. cardiovascular health.
- The safety of some foods with fitness-promoting claims was questioned. Some supplements may be dangerous.
- Supplements were not considered by the Group, but safety was considered to be a pre-condition for any claim.

Synthesis and review of existing processes (ITG D)

Dr David Richardson, Chairman of ITG D, prefaced his presentation of the Group's review by noting that in many countries of the world, a code of practice was evolving, usually voluntary, for validating health claims for food. Moreover, concurrent with the work of the Group, the EC had published a draft proposal for the regulation on "Nutrition, Functional and Health Claims Made for Foods" (SANCO/1832/2002). The Group's objectives had been set as a "critical evaluation of existing international approaches to the scientific substantiation of health claims" and "identification of common ideas, definitions, best practice and a methodology to underpin current and future claims".

The Group summarised, in a table, the regulatory approaches to health claims as set out by seven countries and two international organisations. A common thread in all these approaches is the requirement for scientific substantiation. The need for uniform definitions and meaning of the terminology for "nutritional claims" and "health claims" was stressed. Categories of health claims such as enhanced function and reduction of disease risk formed part of a continuum that does not lend itself readily to division. A distinction was also drawn between "generic claims", which were based on well-established, generally accepted evidence or recommendations from interested bodies, and "product specific claims" which related to an individual food or class of food for which specific evidence should be sought.

The Group focussed on the process of assessing claims, which included identification of all relevant studies, evaluation and interpretation of the totality of the evidence and the concept of "significant scientific agreement". Hierarchies of evidence were specified, details of the design of human studies outlined and the critical evaluation of biomarker use stressed. However, methodological soundness overrides any hierarchy in studies on humans, given that the validity of results depends not only on the appropriateness of the study type but also on the quality of the design, execution and analysis.

In the discussion that followed, important issues were raised.

- Food safety is already regulated, but nutritional safety aspects need further discussion.
- The distinction between a medicinal claim, i. e. for prevention, cure or alleviation of disease and reduction of disease risk is crucial. The EU is proposing to take reduction of disease risk claims on foods out of the scope of medical law.
- The composition of foods with health claims should contribute positively to a nutritionally adequate diet.
- Claims should be consistent with National Dietary Guidelines.
- Claims should be understandable by the intended consumer.
- How will long-term safety be evaluated? Are there plans for post-launch monitoring?
- What will be the process for evaluating claims? How are expert groups to be established in the EU?
- The need for a structured approach to assessing evidence was again brought up. Discrepancy of the outcome of expert groups is detrimental for food development. A process for evaluating scientific evidence must be specified.

Final plenary discussion, day 1

A general discussion followed the ITG reports in which a number of additional points were made:

- The concern of PASSCLAIM is the assessment of scientific support for health claims. Safety, communication and consumer aspects are not relevant here. Safety is already covered by existing legislation. Moreover, there is no methodology for assessing the safety of foods, only ingredients.
- The distinction between generic and product-specific claims is not clear. For example, for plant sterols, would new evidence have to be presented for every type of food in which plant sterols are incorporated or would a generic claim be accepted when a sufficient number of foods to which plant sterols had been added, were tested?
- In Japan, since 1991, over 300 foods have been approved under the FOSHU (Food of specified health use) legislation. Claims are mainly for enhanced function (Type A). New legislation was drafted in 2001. Should EU legislation be harmonised with this?
- Substantiation of claims: What is the level of evidence required? Some existing claims are likely to be true but may not have been demonstrated to be true.
- How can health claims be integrated into existing dietary guidelines? The evidence base for dietary guidelines is often incomplete.

- The distinction between functional foods, for which health claims can be made and foods for particular nutritional uses (PARNUTS) was discussed. It was felt that whilst the distinction was not always clear, functional foods were intended for healthy people whilst PARNUTS are for individuals with specific physiological disorders or diseases. The Commission has recently introduced a new category of PARNUTS (Commission Directive 1999/21/EC) of dietetic foods for special medical purposes. Further special provisions under PARNUTS are envisaged. In practice, a health continuum exists from enhanced function through disease risk reduction to dietetic or medicinal benefits.

First plenary session, day 2

The Chairman, Professor Kok, introduced the session by asking delegates to focus on scientific aspects of health claims. Dr Antoine then presented the draft set of Interim Criteria, which had been drawn up by the steering committee following receipt of the ITG A-D reports (Table 1). The criteria had been divided into three subsets that included 1) Preconditions and Hypotheses, 2) Data and 3) Markers. Under 1) he pointed out that toxicological and nutritional safety was a prerequisite of any substantiation; that the totality of evidence must be considered and target populations identified. A generally accepted and plausible hypothesis should be the starting point. For Data 2), human studies were essential with a valid design, which should be specified. He raised the question of an appropriate control vs. placebo and pointed out that the food approach is different from the drug approach. Data should be reproducible, the food should be consumed in a realistic amount in the context of the total diet and an exposure-response relationship should ideally be demonstrated. When markers 3) are being used, they can be endpoints in themselves, representing a function. Validated markers should be used. He asked delegates to consider what was a significant change, i. e. (statistically significant and physiologically or psychologically relevant?) and to produce a checklist of objective criteria of assessment.

After a short discussion, the delegates were divided into six groups, which then met in working groups with two groups considering each category of evidence (1–3). After two hours of discussion, the plenary session reconvened and the workshop rapporteurs briefed delegates. There was some further discussion, then new workshops were created, with a different delegate mix, but retaining the Chairman and rapporteurs, and a further period was spent discussing the criteria in the light of the comments made in the morning. Finally, the plenary session met again, the workshop rapporteurs came back and there was more discussion. During the day, each set of criteria (1–3) was considered by four separate workshops involving two thirds of the delegates. The main issues raised and recommendations for revising the interim criteria were as follows:

1 Preconditions and hypotheses

- 1.1 There was further debate about whether "toxicological and nutritional safety" was part of the scientific substantiation process and what these terms covered. It was agreed that safety was important and that it included toxicological and microbiological safety. Consumers would need to be assured that safety had been considered. Compliance with existing legislation was an essential precondition for the substantiation process.

  Nutritional safety proved more difficult to debate because there is no clear definition. There was a consensus that it was a necessary precondition but it was felt that the term "safety" did not sit readily with "nutrition". A number of criteria were thought to be relevant to nutritional safety including the effect of the food or food component on the bioavailability of other nutrients, its potential to alter metabolism beyond any claimed effect and its effect on the overall nutritional quality of the whole diet. Long-term safety was also important. Foods for which claims were made must comply with national dietary guidelines, and be part of a healthy diet. In the light of such diverse aspects of nutritional "safety" it was suggested the term "nutritional considerations" be used and defined by us. It was pointed out that in the scientific committee for food of the EU, safety included both toxicology and nutrition.
- 1.2 There was no disagreement with the need to substantiate scientifically all health claims. The meaning of "totality of evidence" was questioned however. Whilst evidence could be drawn from many sources, the requirement for human studies as the primary source was overwhelmingly supported. Human studies included all types of epidemiology, physiological (intervention) studies in healthy individuals, clinical studies where appropriate and sociological and psychological studies. Supporting evidence could come from cellular and molecular experiments, whilst genotyping of individuals would probably become important in the future. Finally, animal studies were considered more appropriate for toxicological work since diet was particularly difficult to model in health studies.

- 1.3 To define a target population was felt to be important because it also defined the relevant groups from which the scientific evidence should be drawn. However, target populations could only be defined once a claim had been clearly stated. A target population could include the whole population, or a subsection defined by age, gender, risk factors for disease etc.
- 1.4 The need for an hypothesis as a precondition for the substantiation process was debated. In nutrition science, research is hypothesis driven. However, the substantiation of a physiological effect by a food or food component requires only the demonstration of the effect, together with its benefit. Whilst a hypothesis was, therefore, felt to be desirable, and might emerge during the substantiation process, it was not thought to be essential. Section 1.4 was deleted because in addition to the statement about a hypothesis, it re-iterated the goal set in 1.2.
- 1.5 Mechanism and hypothesis were discussed. Delegates agreed that they were similar aspects of the same concept. Thus, as for hypothesis, a mechanism was not felt to be essential to the process of substantiation. However, it was acknowledged that mechanisms to explain the effects of food were often known, and might aid in communicating with the consumer. 1.5 was deleted.

2 Data

- 2.6 The emphasis again was on human studies with other sources of evidence, such as animal models, felt to be more valuable for toxicological or mechanistic research.

  The distinction between generic and product-specific claims was debated. Was a different category of evidence required for each? It was suggested that generic claims could be validated by epidemiological studies (cross-sectional, case-control or cohort studies). Generic claims often arose out of Dietary Guidelines. For product-specific claims, human intervention studies were regarded as essential.

  The need for an evidence-based approach to the whole substantiation process was agreed. This methodology was now increasingly being used to judge the benefit of health interventions. It involved a specified and stepwise approach to evidence gathering and the drawing of conclusions. This usually includes:
  - Identification and tabulation of all relevant data (e. g. epidemiology, human trials etc).
  - Assessment of the quality of the evidence, often using a scoring system or by meta analysis.
  - Conclusions based on all available evidence and substantial scientific agreement.

  Such an approach provided for consistency in the substantiation process, is transparent, auditable and allows for much easier updating of evidence.

  Questions were raised about the need to retest products. Would this be necessary if an "active" ingredient for which a claim was made was incorporated into a different food? Similarly, if a minor change in an ingredient or component was made, would this need to go through the substantiation process again?
- 2.7 (a) Statistical power was felt to be important, but self-evident. It should be mentioned at the end of the criteria.
  (b) The representativeness of the study group was accepted. It was noted that genotyping of individuals would become increasingly used in human intervention studies in the future.
  (c) In experimental design careful thought should be given to the reference groups and the dietary controls or comparators. All subjects participating in the study must be representative of the target population, for example in life style (smoking, exercise), and health characteristics. The selection of control diets or interventions for the test food intervention needs similar attention. There may be some advantage, for some interventions and outcomes, in conducting initial studies on selected study populations that would be expected to demonstrate earlier and more clearly the expected outcomes (for example; subjects with diabetes, hypertension, raised blood lipids).
  (d) That intervention studies should be of sufficient duration was accepted but it was not possible, given the expected diversity of such studies, to proscribe this. One suggested guideline was that subjects should be in a steady state metabolically or otherwise, with regard to the food or active principal when measurements of effect were made.
  (e) The meaning of reproducibility was felt not to be clear. Did this mean that two or more identical studies were needed before the effect, which was the subject of the claim, was validated? This was thought to be unrealistic. Generally, it was agreed that reproducibility was not a useful criterion, and that 2.7(e) should be omitted.
- 2.8 The word "ingredient" was not liked, and "food component" preferred. Similarly, "food" was preferred to "product".

Dose-response studies, whilst ideal, were felt to be impractical and were unlikely to be done. In contrast with drug trials, determining the optimal or desirable intakes of functional foods depended on factors that were difficult to control, such as appetite, bioavailability, the confounding effect of other components of the food and the subjects' usual diet. Studies in which intake (dose) of the claimed food or food component was also altered, could prove difficult to interpret.

It was agreed that claims should be based on realistic consumption levels of food or the food component in question. Determining what is realistic is less easy because the diets of individuals vary greatly and their liking for specific foods even more. The principal that the food, for which a claim was being made, should not upset overall dietary balance was felt to be reasonable. However, such judgements could only really be made if the background, or usual diet of the target group was known. This might be a useful prerequisite for any study.

Compliance. There was some limited discussion on this, which was nevertheless felt to be important. In judging the outcome of intervention studies, it is essential to know whether or not the subjects have complied with the protocol, especially with regard to the required intake of test substance. In the event of a study failing to demonstrate a statistically and physiologically significant effect, the question of compliance is crucial. However, measuring dietary compliance is difficult and quantitative markers of compliance (exposure) are few.

3 Markers

It was widely agreed that many outcomes for which health claims might be made had end-points that were unrealistic for human intervention studies. For example, preventing fracture might be a desirable outcome of a functional food, but studies to show this would take many years. Therefore, markers that can predict disease risk or enhanced function were needed. This had been thoroughly discussed during FUFOSE and the consensus document, which proposed a classification and criteria for markers, was the basis for discussion at PASSCLAIM.

- 3.9 The use of markers was endorsed. However, it was stressed that end-points, either of disease risk or enhanced function, would always be preferable and should be measured if possible. Animal studies were sometimes more useful for end-point measures. Markers should be relevant to the health outcome and be indicative of events directly involved in the process relating the food to its effect.
- 3.10 Criteria and validity. The FUFOSE criteria were discussed and generally adopted although with revisions and simplification. The validity of markers was considered to be very important and to comprise several aspects, namely:
  (a) Technical and methodological validity, including accuracy and precision of method, sensitivity and specificity, reproducibility and repeatability.
  (b) Biological validity, which should include its relevance and relationship with health outcomes, the immediacy with which it represented changing events (i. e. should change in a short timescale), and be measured in easily obtained material (i. e. blood, urine, saliva etc).
  - Markers should be used only in studies that had scientifically valid designs.
  - The combination of methodological and biological validity was considered to be included in the term "scientific validity".
  - Markers of exposure were considered to be covered as part of dietary compliance monitoring (see end of Section 2 comments).
  - It was commented that marker validation was often weak. Also that developing and validating biomarkers of effect was a major task and could not really be undertaken by food companies. A database of validated markers could usefully be set up.
- 3.11 The word "intervention" was deleted because markers were equally useful in epidemiological studies.
  - The terms physiological and psychological were both covered by the term "biological".
  - Statistical significance was essential but biological relevance was of overriding importance. Markers must be measured in the target population.
  - Groups of markers may be needed.

After the workshop presentations and discussions, the steering committee and rapporteurs met in the evening to redraft the Interim Criteria. Various options and wordings were presented to the final Plenary Session.

Final plenary discussions

At the final Plenary Session, there was an extended point-by-point discussion of the new Revised Interim Criteria. Many points from previous discussions were emphasised and changes in wording suggested.

The Plenary Session Chairman, Professor Peter Aggett, then summarised the discussions, noting the multidisciplinary nature of the process and that the Criteria were becoming shorter and more concise. He emphasised areas of debate that needed further thought including nutritional considerations, the process for extraction of evidence, the need for markers of exposure (which was an element of bioavailability) and that the development of markers of effect was going to be an educational process for everyone.

The meeting was closed with final remarks from the Chairman of PASSCLAIM, Professor Nils Asp.

Revised interim criteria

Following the meeting, the rapporteurs and steering committee met and it was agreed that the rapporteurs would finalise the wording of the Criteria in the light of all the discussions (Table 2).

Issues that were unresolved at the end of the meeting and require further discussion

- The role of a preamble to the final consensus Criteria, and what should be included in a preamble.
- The meaning of nutritional considerations. In the broader context of nutrition, what boundaries or principles should be set within which the substantiation process should operate.
- A demarcation between functional foods and medicinal products and their relevant claims is needed.
- Type A and B claims: Although the basis for these claims was clearly set out in FUFOSE, there remained doubt in delegates' minds as to the distinction between the two claims. Whilst Type A claims were for enhanced function, they would often imply disease risk reduction. If such a Type A function did not lead to a Type B effect, then it was not necessarily useful. The consumer might expect this.
- A structure for an evidence-based approach to the substantiation process was needed.
- The standard of evidence required for generic as opposed to product-specific claims, should be specified.

Table 2 Revised interim criteria for the scientific substantiation of health claims on foods and food components

1. Foods and food components for which claims are made should comply with existing legislation.
2. Health claims should be scientifically substantiated by taking into account the totality of evidence. A scientifically substantiated mechanism is valuable but not essential.
3. When a claim is made, it should be specified who may benefit from the effect, e. g. the entire population, a subgroup or an at-risk group.
4. Claims should be based primarily on human intervention studies that show demonstrable effects consistent with the claim. They should have a scientifically valid design compatible with the purpose of the study, including the following:
   - Study groups that are representative of the target group
   - Controls both for the intervention itself, and for the subject groups
   - An appropriate duration to demonstrate the intended effect
   - Characterisation of the target groups' background diet, which should be controlled for where necessary
   - The amount of the food or food components being evaluated should be consistent with its intended use and the expected consumption pattern
   - Ideally, an exposure-response relationship should be determined to identify optimum effective intake
   - Dietary compliance, which should be monitored
   - The statistical power to test the hypothesis.
5. If the claimed enhancement of function or reduction of risk cannot be measured, studies should use markers of effect that have been scientifically validated.
6. Markers should be validated:
   Methodologically to include their
   - Precision and accuracy
   - Specificity and sensitivity
   - Reproducibility and repeatability

   Biologically so that
   - They reflect closely the process leading to the claimed health benefit
   - Respond quickly in line with changing events
7. Within a study the marker should change in a biologically relevant way and be statistically significant for the target group consistent with the claims to be supported.