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SUPPLEMENT

The Process for the Assessment of Scientific Support for Claims on Food

Peter J. Aggett

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Abstract The concerted action "The process for the assessment of the scientific support for claims on foods", PASSCLAIM, proposed criteria that could provide an international yardstick for the harmonised transparent assessment of evidence submitted to support a claim for a food or food component. The evidence would be systematically appraised against specific criteria: namely, (1) a characterisation of the food or food component to which the claimed effect is attributed; (2) human data, primarily from intervention studies that represent the target populations for the claim; (3) a dose response relationship; (4) evidence allowing for confounders such as lifestyle, consumption patterns, background diet and food matrix etc.; (5) an appropriate duration for the study; (6) a measure of compliance; (7) adequate statistical power to test the hypothesis. Validated and quality assured markers of intermediate or final outcomes could be used when ideal endpoints are not easily accessible for measurement as long as their relationship to the development of the principal outcome relevant to the claim is well characterised and substantiated. The overall coherence and totality of published and unpublished evidence should be considered in the process. Assessments for substantiation claims need expert judgement, weighting of the strength of the claim, and intelligent use of the criteria applied on an individual basis with respect both to gaps in the knowledge and to any need for new knowledge and data.

Keywords Diet · Claims · Food and health · Markers · Health claims · Biomarkers

The ILSI (Europe) coordinated European concerted action on Functional Food Science in Europe (FUFOSE) which ran between 1995 and 1997 developed a working definition of functional foods and reached a consensus on the scientific evidence needed to demonstrate that such specific foods or food components actually had positive or beneficial affects and physiological functions by enhancing or sustaining systemic biochemical and physiological functions, reducing the risk or delaying the onset of disease, and improving well-being and psychological function, either separately or in any combination of these [1]. It was appreciated that such benefits need to be shown to be genuine. This is the essence of evaluative and evidence based science whether it is in nutrition or in any other discipline exploring the outcomes and responses to intakes of exogenous compounds.

FUFOSE critically assessed the science base required to demonstrate that specific foods or food components positively affect target functions in the body. It did this from a perspective of needing objectively demonstrable functional outcomes, rather than speculative submissions supporting products based on evidence created by extrapolating from generic evidence and weak epidemiological associations, perhaps bolstered by eager advocacy. FUFOSE reached a consensus on how specific functional claims might be explored and justified, and identified areas in health and well-being that might benefit from targeted scientific approaches to the generation and evaluation of functional foods. The concerted action produced the familiar "egg

On behalf of the EU PASSCLAIM concerted action.

Please direct all correspondence to: ILSI Europe a.i.s.b.l, Avenue E. Mounier 83, Box 6, 1200 Brussels, Belgium.
E-mail: publications@ilsieurope.be

P. J. Aggett (✉)
Lancashire School of Health and Postgraduate Medicine, University of Central Lancashire, Preston PR1 2HE, UK
e-mail: profpjaggett@aol.com

diagram" (Fig. 1) showing a chain of markers of exposure, body burden, intermediate effects and the final beneficial outcome. This emphasised the interrelationship of markers of exposure and effect, their mechanistic connections and their associated dose response relationships. This highlighted the strategic use of a series of valid and quality assured markers to create an objective evidence base for the justification of health claims [3].

A claim has been defined by the Codex Alimentarius in 1979 as "any representation which states or implies that food has certain characteristics relating to its origin, nutritional properties, nature, production, processing, composition, or any other quality" [1, 3]. The current situation relating to the types of claims that may be made is a principal focus of this meeting so I would just comment that at the time when the PASSCLAIM activity was evolving the categories of claims were broadly seen as addressing "what the product contains: for example nutrient content claims (low-fat, fat-free, low sugar, source of fibre, high fibre, high protein, high in vitamins, high in minerals etc.), or what the product does expressed in relation to a well-established end function which would perhaps be the basis of a generic functional claim, or a claim for enhanced function, or a reduction of disease risk.

PASSCLAIM had three basic objectives [1]; these were to

1. evaluate critically existing schemes that assess scientific substantiation of claims
2. produce a generic guidance tool for assessing the scientific support for health claims for foods
3. establish criteria which can be used to explore the links between diet and health.

The Concerted Action drew on and critically evaluated investigative studies that were used to underpin existing claims, and, also, current practice and regulatory and advisory processes for evaluating and approving claims.

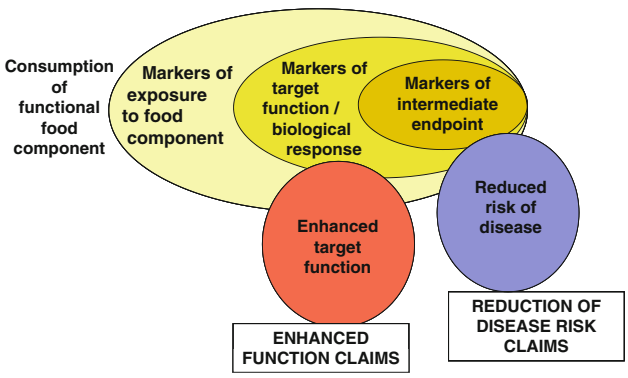

Fig. 1 The FUFOSE strategic scenario of markers for use in the scientific support of claims for foods [3]

The activity collated potential types of claims and described the scientific support needed and evaluated the relevance of this. Drawing on this practice, and on the concepts developed as part of FUFOSE, the activity assessed the use and validation of markers. From this it developed a list of criteria that could be used to evaluate any database being submitted for the substantiation of claims. In the first set of activities three thematic working groups explored actual and potential claims on their evidence base in (1) diet related cardiovascular disease [4], (2) bone health and osteoporosis [5] and (3) physical performance and fitness [9], and a fourth thematic group reviewed existing processes for claims and their review and regulation [8]. The experience and recommendations of these four groups were then applied to derive an interim set of criteria for the evaluative framework. This and the lessons learnt from the first activities were then applied by four further thematic working groups that are considered (1) insulin sensitivity and diabetes mellitus [7], (2) diet related cancer [6], (3) mental state and performance [10] and (4) gastrointestinal function and immunity [2]. After a second plenary meeting a consensus group prepared a final report which was refined after a third plenary meeting [1].

Overall the PASSCLAIM exercise represented an effective precompetitive collaboration involving representative stakeholders involving 45 participants from Universities or Research Institutes, 63 from the Food Industry and 83 from consumer and public interest groups, and regulatory and legislative authorities.

The PASSCLAIM criteria for the scientific substantiation of claims are listed in below [1]:

(1) The food or food component to which the claimed effect is attributed should be characterised.
(2) Substantiation of a claim should be based on human data, primarily from intervention studies, the design of which should include the following considerations:
    (a) Study groups that are representative of the target group
    (b) Appropriate controls
    (c) An adequate duration of exposure and follow-up to demonstrate the intended effects
    (d) Characterisation of the study group's background diet and other relevant aspects of lifestyle
    (e) An amount of the food or food component consistent with its intended pattern of consumption
    (f) The influence of the food matrix and dietary context on the functional effect of the component
    (g) Monitoring of subjects' compliance concerning the intake of the food or food component under test.

(3) When the true endpoint of a claimed benefit cannot be measured directly, studies should use markers.
(4) Markers should be: biologically valid in that they have a known relationship to the final outcome, and have a known the variability within the target population; methodologically valid with respect to their analytical characteristics.
(5) Within the study the target variable should change in a statistically significant way and the change should be biologically meaningful to the target group consistent with the claimed to be supported.
(6) A claim should be scientifically substantiated by taking into account the totality of the available data and by weighing of the evidence.

There are some basic assumptions which provide the context for the application of these criteria. These are; that the foods and food components for which a claim is made should comply with existing legislation (for example those relating to safety); that they would and should be consumed as part of a healthy diet; that the regulatory environment should reflect and accept the evolving science base, and thus be prepared to take into account new scientific developments as appropriate; and that any claim should reflect its scientific basis and be understandable to consumers and not mislead them.

The pathway and markers shown in Fig. 1 summarises the evidence based approach to nutrition and metabolism [3]. It demonstrates that the desirable outcome may be removed both in time and in terms of the physiological and biochemical mechanisms from the consumption of the food component. This, in turn, would necessitate the use of intermediate or surrogate markers as for the potential "outcomes". The identification of these intermediate markers requires an informed insight of the relevant mechanisms and an intelligent selection and evaluation of an appropriate marker from what might be a large number of candidate markers. Therefore, the validation and quality assurance of any selected marker is particularly important if it is going to contribute to the substantiation of the claim and not be misleading both to the investigators and to consumers [1, 3].

The criteria reflect an appreciation that any claim for a food or food ingredient or dietary supplement should be based on evidence derived principally from human studies that represent expected use of the product in the context of a usual diet. Studies in animal models may underpin the mechanistic plausibility and any claimed causal association, as well as informing the identification and validation of intermediate markers for use when ideal endpoints are not accessible. Even so, data from animal models are not substitutes for human based data with clear dose–response relationships with outcome markers that have a proven validity and quality assurance in humans. As such, markers could be used for many biomedical outcomes, including mental and physical performance, and mental health and well-being [1, 10].

The evidence in support of the claim can come from many sources and ideally it should build a portfolio that substantiates an objective and verifiable case. Thus epidemiological or natural surveillance data can be used to demonstrate associations, identify markers, characterise study populations and to generate hypotheses. Data derived from studies on animal models can, as has been said, be supportive in generating hypotheses and associations, and through the exploration of mechanisms, can enable the identification of markers processes and intermediate outcomes. A claim can not be based solely on data from animal studies, or on in vitro or molecular investigations, or on observational or anecdotal information which would be unlikely to be substantiated without any intervention study. However, all this information overall can provide a sound background or platform for the definitive study that would substantiate the claim. Thus although observational human studies would be unlikely to justify a sound claim, their data would help characterise potential participants for the definitive interventional studies and they would also identify possible beneficiaries for the claimed effect, and, additionally provide clues about suitable candidate outcomes and potential surrogate markers.

The portfolio of evidence collectively should provide evidence of consistency of results across the various categories of evidence and methodologies. It should be evident that valid dietary methods have been used to monitor intakes and exposure to the food or food component in question, and that compliance has been good. Clear dose response relationships or threshold exposure for effects, between intakes of food and food components and the effects should be apparent, and in general the data should show biological plausibility. Importantly, given the variance of intake data and of the chosen outcomes it should be evident that the intervention studies have been appropriately randomised and have sufficient power.

All appropriate data should be included in the portfolio of evidence. Selective presentation and inclusion of studies in a portfolio is only acceptable if this is done transparently on the basis of the quality of the data, rather than on the nature of the study outcomes. Essentially, all published studies should be reviewed as part of the portfolio and, ideally, any relevant unpublished data, including those that are being withheld from publication for reasons of confidentiality should also be considered. However, this would be difficult to enforce and would probably remain an ideal rather than a definite requirement for any portfolio of evidence.

The PASSCLAIM criteria were drawn up as a yardstick or a gold standard. The activity consensus deliberately avoided setting up any algorithm or scoring system that might enable a quantitative expression of the strength of the scientific evidence submitted in support of a claim. It was felt that the criteria could serve as a universal standard that would enable international and interagency harmonisation and transparency of approaches to establishing claims. Given the relatively uncompromising standards set by the criteria it is probably best left to competent authorities who can on a case-by-case basis perform a risk–benefit analysis of any portfolio for a claim. Thus the PASSCLAIM consensus has made no recommendation on how a claim based on the evidence should be weighted; i.e. graded as "convincing", "probable", "possible" or insufficient, or graded on a scale from A to D. The flexibility of any system to allow or qualify claims should lie with the competent authorities acting on the advice of its stakeholders as part of a risk–benefit analysis of the claim. The criteria offered by PASSCLAIM provide a basis of scientific integrity. Even though the criteria applied specifically to the assessment of a portfolio of submitted evidence and are not meant to provide a template for a research strategy if any product, it was appreciated and hoped that those who are responsible for compiling and acquiring the scientific support for claims would be able to use the criteria as a guide.

It is envisaged therefore that the advisory and regulatory process for the review of scientific portfolios will need informed scientific advice to support an intelligent interpretation of the evidence and its ambiguities and uncertainties, and to enable a transparent extrapolation, or otherwise, of data to other age and gender groups. Such expert evaluation would be needed to advise on whether or not claims have drawn on the full spectrum of scientific data, whether or not the portfolio shows the best of current knowledge, the totality, consistency and complementarities of existing evidence, and to decide whether or not questions that the submission may leave unanswered need to be answered by additional research, or whether the overall evidence compensates these gaps.

PASSCLAIM did not consider how agencies would pass the assessment into national or supranational decision making processes. Nevertheless the criteria would enable any other stakeholders that might be engaged at this stage to understand the nature of the scientific evaluation of the evidence submitted to support the claim. Thus overall the criteria should facilitate and enhance the efficiency of regulatory review, evaluation and feedback to all involved not least those seeking approval for a claim.

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