The evaluation of health claims in Europe
What have we learned? – Part 2

IGOR PRAVST
Nutrition Institute, Nutrition and Health Claims Support Unit
Vodnikova cesta 126
Ljubljana, SI-1000, Slovenia

Igor Pravst

KEYWORDS: Health claims, scientific substantiation, functional foods, food supplements.

ABSTRACT: In the last issue we discussed the implementation of health claims legislation in the European Union (1) and focused on techniques for boosting the chances of success with health claims applications. In relation to this, it is very important to learn from the EFSA's existing opinions to avoid problems which have already surfaced. In the first part, the impact of health claim wording was examined with some examples, while the sufficient characterisation of foods or food constituents, specific conditions of use and the target population, the relevance of the claimed effect on human health and the overall quality of human studies for a successful scientific substantiation of the claimed effect is presented below.

FOOD CHARACTERISATION

The sufficient characterisation of foods or food constituents is very important not only for the proper scientific evaluation of a health claim application, but should also allow control authorities to verify that a product which bears a claim is the same one that was the subject of an authorisation (2). In the scientific evaluation process the characterisation is needed to identify the food or food constituent, define the appropriate conditions of use, and to connect it with provided scientific studies (2). These studies should be performed using the same food or food constituent and must also include suitable characterisation. The lack of characterisation is one of the most common reasons for the EFSA's non-favourable opinions regarding general function claims.

In relation to characterisation it may be necessary to distinguish between a specific formulation, specific constituent and a combination of constituents (2). All combinations must be characterised in detail, particularly in relation to the active constituents. Beside physical and chemical properties and composition, it is also beneficial to specify the analytical methods applied (2). In cases where variations in composition could occur, it is also valuable to describe the manufacturing process and provide the results of studies of the variability from batch to batch and stability with respect to storage conditions during shelf life. Where applicable, it is useful to show that a constituent is bioavailable or provide a rationale that target site is reached by constituent (2).

For microorganisms genetic typing should be performed at the strain level by internationally accepted molecular methods and the naming of strains according to the International Code of Nomenclature. The EFSA has suggested the voluntarily deposit of a sample in an internationally recognised culture collection for control purposes (2). Applicants should also provide evidence of the stability of the microorganisms and influence of the food matrix on their activity. The lack of such evidence might well constitute a reason for the EFSA's negative opinion. Such an example is a health claim application for a probiotic food supplement containing freeze-dried lactic acid bacteria (3) where no studies were provided on the impact of the food matrix on the viability and activity of the lactic acid bacteria.

For plant products the scientific name of the plant should be specified, together with that part of the plant used and details of the preparation used, including details of the extraction, drying etc. It is beneficial when the applicant can show that the composition of the plant-derived product can be controlled by analyses of specific chemical ingredients. For example, a lycopene-free water-soluble tomato concentrate was recognised as having been successfully characterised on the basis of a clearly described production manufacturing process from tomato (*Lycopersicum esculentum*) together with detailed chemical specifications and demonstrated batch-to-batch reproducibility (4). Chemical compounds which have been shown to have a beneficial effect *in vitro* were identified and quantified using the HPLC-MS technique, and the presence of unspecified constituents was limited. Several chemical and physical characteristics were assessed during stability testing, including breakdown products and the microbial status. Bioactive components were shown to survive and to retain their activity *in vitro* over typical product shelf lives when the product was included in specified matrixes (fruit juices, fruit flavoured drinks and yoghurt drinks) (4). Another useful example is a general function claim application for honey in connection with its effects on respiratory health. It was considered that honey may contain different active ingredients depending on the source of the nectar and the species of the bee which might affect the proposed health relationships. The result was that the food, honey, was not sufficiently characterised (5).

Specific conditions of use

The quantity of the food or food constituent and pattern of consumption must be specified together with possible warnings, restrictions on use and directions for use. It is important that the consumer can consume enough food as part of a balanced diet to obtain the claimed effect (6). The applicant must also specify the target population. In connection with this, it is critical that the specific study group in which the evidence was obtained is also representative of the target population for which the claim is intended (6). A critical question is whether the results of studies from patients can be extrapolated to the target population. It is now clear that this judgement is made on a case-by-case basis. If studies were not performed on a representative of the target population the applicant must provide evidence that the extrapolation can be performed (2). By learning from existing scientific opinions we can see that patients are not an appropriate study group in most cases. For example, the results of studies on patients with a diagnosis of rheumatoid arthritis (7) or osteoarthritis (8) cannot be used for joint health claims. The EFSA noted that no scientific conclusions can be drawn from

studies on patients with genetically and functionally different cells and tissues. In addition, in the evaluation of a disease risk reduction claim application for lycopene and its effect on preventing oxidative damage of plasma lipoproteins in relation to reducing the build up of arterial plaques and consequently the risk of heart disease it was disclosed that the results of studies on coronary heart disease patients cannot be extrapolated to the general population, at least not without additional evidence being provided (9). Nevertheless, in some cases studies in patients can be considered as pertinent. For example, studies in patients with irritable bowel syndrome may be accepted for claims on reducing gastro-intestinal discomfort in the general population (2). This was also shown in the case of an application for prebiotic, where such studies were considered as relevant (10). Studies on untreated hypertensive subjects were also accepted in the scientific substantiation of a general function claim application for the role of long-chain omega-3 polyunsaturated fatty acids in maintaining normal blood pressure (7). Further, overweight and obese volunteers could be used for studies with products targeting weight management despite the fact that obesity is a medical condition. In a recent opinion regarding the *Caralluma fimbriata* extract a body weight reduction study on overweight and obese subjects was considered as pertinent (11), but no cause-and-effect relationship was established for other reasons.

Relevance of the claimed effect

The claimed effect should be clearly defined and relevant to human health. This can be demonstrated with the already mentioned example of the *Caralluma fimbriata* extract, and its effect on one's waist circumference (12). The applicant provided studies showing a statistically significant reduction in waist circumferences, but it was concluded that a reduction in one's waist circumference is not a beneficial physiological effect if it is not accompanied by an improvement in the adverse health effects of excess abdominal fat.

In another new general function claim application, no cause-and-effect relationship was found between the consumption of a specific prebiotic product and the maintenance of a normal gastro-intestinal function even though studies had demonstrated a significantly increased number of bifidobacteria in the gut. It was concluded that there was no evidence provided that changes in the number of bifidobacteria in the gut are beneficial for the gut function (10). On the contrary, only a slight improvement in parameters which are widely accepted as important to human health can be recognised as critical evidence, such as in the case of a general functional claim for the role of omega-3 in maintaining normal blood pressure (7). The EFSA concluded that high doses (3 g per day) of docosahexaenoic (DHA) and eicosapentaenoic acid (EPA) may have smaller, but statistically significant, effects in normotensives of about 1 mmHg; better results were observed in subjects with untreated hypertension.

SCIENTIFIC SUBSTANTIATION OF THE CLAIMED EFFECT

Human data are critical for substantiating a claim and particular attention is paid to whether such studies are pertinent to the claim. Pertinent studies are studies from which scientific conclusions can be drawn for the substantiation of the claim, meaning that studies have been carried out with the subject product with similar conditions of use in a study group representative of the population group and using an appropriate outcome measure of the claimed effect (13). Using appropriate outcome measures can be a challenge

because a limited number of validated markers is available (14). Biomarkers are characteristics that are objectively measured and evaluated as indicators of normal biological processes, pathogenic processes or pharmacologic responses to therapeutic intervention (15) and must be clearly distinguished from risk factors which are independent predictors of the development of human disease (i.e. elevated low-density lipoprotein blood cholesterol is a recognised risk factor in coronary heart disease).

In the health claim application the totality of the available scientific data should be provided, including unpublished results and studies showing no effect or opposing effects (13). Well-performed human intervention trials are particularly important for successful substantiation. Double-blind, randomised, placebo-controlled trials are considered the *gold standard* not only for the substantiation of disease risk reduction claims but also for general function claims. During the scientific evaluation such trials are assessed critically to assure there are no weaknesses. A good study design, proper performance, well-defined statistics and appropriate statistical power (enough subjects) are critical in this context. It is also important to note that the results of trials performed in outsourced reliable clinical research organisations according to good clinical practice (GCP) might be more trustworthy than results performed in questionable conditions. In some cases, non-blind studies are also acceptable, particularly in the case of non-processed foods where blinding is impossible. This was confirmed recently in the case of a general function claim application for dried plums in connection to maintenance of bowel regularity, and a laxative effect (16). A study in which subjects free of gastrointestinal and eating disorders were randomised to consume either dried plums or grape juice was found to be pertinent. Nevertheless, taking the results of other studies into account there was insufficient evidence to establish a cause-and-effect relationship.

Human observational studies and data from studies in animals or model systems are only considered as supporting evidence (13).

ESSENTIAL NUTRIENTS

When talking about essential nutrients we need to consider that there is a well-established consensus among scientific experts on many functions of such nutrients. In a recent briefing document the EFSA noted that the Panel may rely on such a consensus and that, in such cases, it may not be necessary to review the primary scientific studies on the claimed effect of the food (2). Such a procedure has mainly been used for general function claims concerning vitamins and minerals.

A STEEP LEARNING CURVE

Today it is clear that the implementation of health claims legislation has involved a steep learning curve which is far from complete (17). After the EFSA's first evaluations were published, particularly in connection with widely used general function claims, the industry was very critical of an Authority which used the same scientific standards for all types of claims. It is no surprise that at the same time responses from consumer organisations were very positive. Indeed, one of the primary roles of the regulation is to protect the consumer, yet this must not happen at the cost of innovations leading towards healthier diets. It is clear that the labelling and presentation of foods must not be misleading and claims must be supported by valid scientific evidence, but we should also consider that most food producers are not used to performing human trials with near-pharmaceutical standards and that, in many cases, it is unclear what kind of evidence is needed to have claims substantiated. While the EFSA has had to cope with an unprecedented and unforeseen workload, coupled with very short deadlines (17) , the industry is financing very expensive trials which are often still not being performed using standards that would enable successful substantiation. To overcome this problem we should offer greater support to the industry to assure that trials are performed appropriately. More dialogue is needed between the industry representative and risk manager, particularly during and after the assessment phase (18-20). The EFSA's decision to organise workshops in selected areas, i.e. on gut and immune function, envisaged in December 2010, has therefore been very well accepted by industry, although many companies are afraid this will be too late to have their general function claims approved.

REFERENCES AND NOTES

1. I. Pravst, *Agro Food Industry Hi-Tech*, **21(4)**, pp. 4-6 (2010).
2. *EFSA, Briefing document for stakeholders on the evaluation of health claims*, May 2010, Parma, Italy.
3. *The EFSA Journal*, **782**, pp. 2-2 (2008).
4. *The EFSA Journal*, **1101**, pp. 1-15 (2009).
5. *EFSA Journal*, **8(2)**, p. 1484 (2010).
6. *The EFSA Journal*, **530**, pp. 1-44 (2007).
7. *EFSA Journal*, **7(9)**, p. 1263 (2009).
8. *EFSA Journal*, **7(10)**, p. 1358 (2009).
9. *The EFSA Journal*, **1179**, pp. 1-10 (2009).
10. *The EFSA Journal*, **1107**, pp. 1-10 (2009).
11. *EFSA Journal*, **8(5)**, p. 1604 (2010).
12. *EFSA Journal*, **8(5)**, p. 1602 (2010).
13. *EFSA Journal*, **7(11)**, p. 1386 (2009).
14. M. Cazaubiel, J.M. Bard, *Agro Food Industry Hi-Tech*, **19(5)**, pp. 22-24 (2008).
15. NIH Biomarkers Consortium (http://www.biomarkersconsortium.org/, accessed May 2010).
16. *EFSA Journal*, **8(2)**, p. 1486 (2010).
17. Technical meeting: EFSA health claims evaluation under Regulation (EC) No 1924/2006, June 2010, Parma (http://www.efsa.europa.eu/en/edspeeches/speeches/parma100601.htm, Accessed: June 2010).
18. Frewen M; Health Claims: Experiences and Mella Expectations from Industry; EFSA Technical Meeting on Health Claims, June 2010, Parma.
19. P. Coppens, *Agro Food Industry Hi-Tech*, **21(2)**, pp. 24-26 (2010).
20. P. Coopens, *Agro Food Industry Hi-Tech*, **21(3)**, pp. 6-8 (2010).

ONE BLEND. TRIPLE ACTION.

CLINICALLY STUDIED: Reap the benefits of patented natural extracts ForsLean® and GarCitrin® in a naturally bioavailable composition with BioPerine®. Phytonutrients forskolin, hydroxycitric acid, and garcinol work together to support lean body mass, satiety, energy level, and a healthy body weight and composition. LeanGard was evaluated in a randomized, double blind, placebo controlled study with 50 obese subjects. When compared to baseline values, a 500 mg daily intake of LeanGard® for 12 weeks effected a statistically significant mean decrease in BMI of 7.45%, and waist:hip ratio of 6.47%; body fat reduction of 8.15%, and an increase in lean body mass of 4.36%, with no untoward side effects. Experience this triple action blend today.

Sabinsa Europe GmbH
www.sabinsaeurope.com | sabinsa.europe@sabinsa.com
Tel: +49 6103 2701111 | Fax: +49 6103 2701127