MNF Report

Criteria for the evaluation of functional foods

*Opinion of the Senate Commission on Food Safety (SKLM) of the German Research Foundation (DFG) – (shortened version)**

Gerhard Eisenbrand

Lebensmittelchemie und Umwelttoxikologie, Technische Universität Kaiserslautern, Kaiserslautern, Germany

Preamble

The Senate Commission on Food Safety (SKLM) of the DFG has elaborated the following recommendations entitled "Criteria for the Evaluation of Functional Foods" with the objective of defining the minimum requirements for the evaluation of the safety to health of functional foods (FFs) and for the scientific proof of their functionality. [...]

Differentiation of functional foods from other foodstuffs and products

Functional foods

No legally binding definition exists as yet for FFs. The SKLM therefore relies on the definition described in a consensus document elaborated in the context of an EU initiative, the so-called FUFOSE working group. According to this definition a foodstuff may be considered as being "functional", if it exerts a demonstrable positive effect beyond its normal nutritional physiological effects on one or several target functions in the human body, thereby achieving an improved state of health or an increased feeling of wellness and/or a reduction in the risk of developing a disease. FFs are offered for sale exclusively in the form of foodstuffs and not, as are food supplements, in the form of medicinal preparations resembling medicines. They must be an integral component of normal nutrition and should already exert their effects when consumed in normal amounts. [...]

Correspondence: Prof. Dr. Gerhard Eisenbrand, Lebensmittelchemie und Umwelttoxikologie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Str., D-67663 Kaiserslautern, Germany
E-mail: eisenbra@rhrk.uni-kl.de
Fax: +49-(0)631-205-3085

A FF may be functional for the whole population or only for a defined population group (*e.g.* defined by age or genetic constitution).

Foodstuffs enriched with certain nutrients

According to the definition of the Codex Alimentarius Commission foodstuffs enriched with certain nutrients are foodstuffs to which essential nutrients, i.e. substances for which generally accepted intake recommendations exist, have been added as enrichment or supplementation with the aim of preventing a deficiency of one or several nutrients in the general population or only in certain population groups. Such a modification of a foodstuff, covered by accepted nutritional recommendations as issued by societies recognized as peer advisory bodies in this field, does not provide any functional effects over and above those of normal nutrition that could be identified by the criteria described below. Therefore, simple enrichment with essential nutrients cannot be regarded as a functional principle within the meaning of definition for Functional Foods mentioned above. Similar considerations apply to any reductions in the content of any food component.

* *Deletions in the original text are labelled by "[...]" For more information, please refer to the original document (Deutsche Forschungsgemeinschaft Kriterien zur Beurteilung Funktioneller Lebensmittel / Criteria for the Evaluation of Functional Foods – Sicherheitsaspekte / Safety Aspects, Symposium / Abridged Version, Published by the Senate Commission on Food Safety, Wiley-VCH Verlag, Weinheim 2004, 67 pages, ISBN 3-527-27515-0; or the full version: Deutsche Forschungsgemeinschaft, Functional Food – Safety Aspects, Symposium Volume, published by the Senate Commission on Food Safety, Wiley-VCH Verlag, Weinheim 2004, 384 pages, ISBN 3-527-27765-X). Also references to the literature of the original document are not included.*

Food supplements

Food supplements are defined in a Draft Directive of the European parliament and Council as foodstuffs consisting of concentrates of single or multiple nutrients, marketed in the form of dosed preparations and destined to supplement the intake of these nutrients within the scope of normal nutrition. In this draft the concept of nutrients encompasses merely vitamins and minerals. "In the form of a dosed preparation" signifies a form of preparation similar to medicines, *e. g.* capsules, tablets, pills, ampoules.

Evaluation of the safety to health

General requirements

FFs must not be a hazard to the health of the consumer and it is required that they be thoroughly investigated and evaluated in this respect. Targeted investigations of their functional effects in humans may only be initiated when no indication of a risk to health is apparent in the light of current knowledge.

Any safety evaluation should comply with the guideline recommendations for novel foods of the EU Scientific Committee on Food (SCF), independent of whether the FF does or does not fall within the scope of the definition in the EC-Directive Nr. 258/97 and any subsequent amendments concerning novel foodstuffs and novel food ingredients. [...]

A FF usually differs from its comparable product either by the presence or absence or an increased or reduced concentration or bioavailability of one or several functional components. It is possible in such circumstances to restrict the safety evaluation to the functionally effective ingredients. If necessary, the additional influence of the matrix of the foodstuff has to be considered. [...]

The nature and extent of the required investigations depend on the properties of the functional components or active principle and also on the expected future exposure of the target population or the potential population group at risk. It is essential to prepare a systematic summary of the entire available information on the properties of the functional components and their possible adverse effects. [...]

Single substances, mixtures of substances and extracts

The SKLM recommends that the testing requirements for the evaluation of the safety to health of functional ingredients should follow internationally recognised testing criteria for food additives as published in "Guidance on submissions for food additive evaluations by the Scientific Committee on Food" (opinion expressed on 11 July 2001, http://europa.eu.int/comm/food/fs/sc/scf/out98_en.pdf).

Essentially, the requested information includes an adequate characterisation of the functional ingredients, *i. e.* a description of their chemical composition, their physico-chemical and microbiological properties, their sources, and the processes employed for their isolation or production. Additionally, specifications, purity criteria and practical methods of analysis must be provided. Information must be supplied on their stability in the foodstuff, their possible degradation and reaction products and on possible interactions with nutrients and any influences on the bioavailability of these nutrients.

For the safety evaluation the basic data listed in the aforementioned SCF guidelines must be submitted. In certain cases it may be necessary to perform supplementary studies as described in the guidelines.

Enzymes

If pure enzymes or enzyme preparations are added as functional components over and above their use for purely technological purposes, the SKLM recommends that the testing criteria chosen for the safety evaluation should be defined within the context of a case-by-case consideration according to the guidelines mentioned below:

- Guidelines of the SCF for the presentation of data on food enzymes (opinion expressed on 11 April 1991, http://europa.eu.int/comm/food/fs/sc/scf/reports/scf_reports_27.pdf);
- Recommendations of the SKLM on the evaluation of starter cultures and enzymes used in food technology (DFG 1987, ISBN 3-527-27363-X);
- Recommendations of the SKLM on the evaluation of novel proteins, which may enter foodstuffs through the use of genetically modified plants (SKLM opinion expressed on 2/3 June 1997).

According to the SCF guidelines information is required on the source of the enzyme, the method of production, the catalytic activity, the stability in the food product, and the intended use of the product. For the safety evaluation of enzymes of different origin the basic toxicological data listed in the SCF guidelines must be submitted for each individual enzyme.

Also, as the catalytic function of the enzyme may cause not only changes in the foodstuffs but also in the digestive processes and in the bioavailability of nutrients after uptake from the intestinal tract, this aspect has to be examined.

According to the recommendations of the SKLM evidence for the safety to health must be provided in the form of a case-by-case consideration using a combination of various investigations. These may include comparisons for homol-

ogy with toxic proteins and allergens. Furthermore, information is needed on the degradability of the enzyme protein in the gastro-intestinal tract.

Cultures of microorganisms

Whenever the functionality of a functional food depends on the presence of cultures of microorganisms, the SKLM recommends that the testing criteria for the evaluation of the safety to health should be in accordance with the following recommendations and guidelines:

- Recommendations of the SKLM on starter cultures and enzymes for food technology (DFG 1987, ISBN 3-527-27362-X);
- Recommendations of the BgVV on cultures of probiotic microorganisms in foods (http://www.bgvv.de/cm/208/probiot.pdf);
- FAO/WHO guidelines for the evaluation of probiotics in foodstuffs (http://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf).

Preferentially strains of such species should be used that during their traditional long-term employment in food production have proven themselves to be safe for consumption by man or to be commensals in the human intestinal tract. It is necessary to characterize the taxonomic position and to provide information on the possible infectivity, virulence and persistence. [...]

In addition, tests may become necessary for specific, potentially adverse metabolic activities or properties. Examples would be the formation of biogenic amines or of toxins, the activation of pro-carcinogens, an influence on blood coagulation or a possible haemolytic activity, the induction of allergic reactions as well as effects on the immune system.

Functionality and claims

A FF must produce – according to the intended claim – one or several effects which exceed those that may be achieved by a comparable product consumed in comparable amounts as part of a balanced diet.

Evidence for a special effect is the precondition for any desired claim. A claim represents the linguistic description of product-specific properties which extend beyond the properties of a comparable foodstuff. This claim serves as the basis for defining the type and extent of the necessary studies.

For the scientific proof of any functionality it is necessary to carry out prospective studies in humans after assurance of the safety to health. Evidence of the claimed effect should be produced for the product under examination. For the scientific proof of functionality a study hypothesis must be formulated a priori. Preliminary pilot studies are frequently useful for deciding about the final study design and the targeted parameters, analogous to requirements in.

In this connection the type and extent of the necessary studies in humans are to be determined depending on the actual FF, its functional principle, and the intended claim. A minimum of two independent studies is desirable, of which at least one human study is essential, preferably following the design of a controlled, randomised double-blind study against a non-functional comparable product. [...]

Although, the type and extent of studies with FFs may deviate from those performed for medicines, yet their quality, as concerns concept, execution and evaluation must not be lower than that required for the testing of medicines. [...]

The studies should be so designed that they also record undesirable effects. In order to estimate reliably the type and extent of adverse effects a sufficient number of observations on sufficient subjects are needed. The SKLM recommends that the demonstration of a functional effect with probiotic foodstuffs should follow the criteria of the BgVV-working group "Probiotic microorganism-cultures in Foodstuffs" (http://www.bgvv.de/cm/208/probiot.pdf).

Important quality criteria for human studies to demonstrate the functional effect of a food are listed as key phrases:

- procedure to follow a hypothesis
- prospective character
- test parameters for the effect to be fixed in advance of study
- control groups
- study plan
- biometry
- adequate power of the study
- informed consent of participants, agreement of ethics commission
- randomisation
- double blind study
- stratification according to factors influencing the functional effect, e.g. age, sex, nutritional status, health status, other parameters defining the chosen endpoints.
- criteria for discontinuing the study
- compliance, i.e. maintaining the amounts consumed and the consumption frequency as well as documentation of the parameters (concordance)
- limited default rate for participants in the study group
- adequate biometric evaluation
- monitoring to confirm the quality of the diet
- accounting for adverse reactions
- report of results of the study to follow recognised criteria; CONSORT statement

Frame I

Questions which are of paramount importance in the evaluation of the relevance and validity of the results:

- Have all relevant findings and knowledge contained in the available literature and other sources been appropriately considered and according to which criteria were they collected?
- Are the results of the studies directly correlated with the hypothesis?
- Is there evidence for the observed functionality also from experimental studies in animals?
- If the finding concerns an effect on a so-called surrogate biomarker, has the relationship of the surrogate biomarker to the hypothesis been ascertained and validated?
- Is the group of individuals examined representative of the target population group for the product?
- Does confirmation exist of the nature and strength of the effect through one or more studies carried out according to recognised criteria?
- Do comparable studies exist with negative findings?
- Are long-term changes of the test parameters included among the observations with special attention being paid to adaptive responses of the organism to or reversibility of the effects?

Frame II

Observation after market introduction

The procedure for post-marketing observation must be suitable for sampling the actual consumer groups and measuring the amounts actually consumed. On the basis of these data a comparison should be made between the actual and the expected amounts consumed and of the specificity of the product for the target population. After placing on the market of a FF it is sensible to determine the functional effects and any potential undesirable effects appearing as a consequence (post-launch monitoring).

Concluding remarks

The SKLM has assembled together these criteria for the evaluation of the safety to health of FFs as well as for the scientific proof of their functional effects in conformity with the state of knowledge in 2002. The SKLM is aware that this opinion will require constant updating according to the state of the science existing at the relevant time. [...]

