

COMMENTS
in relation to the third batch of Article 13.1 claims opinions

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European Commission
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Re: Comments to the third Batch of EFSA opinions as published on 19 October 2010

Dear Mr Mathioudakis,

First of all we would like to thank the European Commission for the openness and the professional way in which it has addressed the many problems the implementation of the Nutrition and Health Claims Regulation (NHCR) has created and has considered comments made by us in previous communications. In particular, we see the opportunity to provide further information on insufficiently characterised or substantiated claims, the abandoning of the batchwise adoption of the Article 13 list and the separation of botanicals until a number of issues are resolved as very important and clear signs that the EC is aware of the difficulties the process has created and is actively looking for measures that can bring the process again within its originally intended objectives. We continue to offer our help and input in this process.

We herewith take the opportunity to provide you with our comments in relation to the third batch of EFSA opinions, published on 19 October 2010 relating to the Article 13.1 list. We have performed a detailed assessment of the opinions and would like to share our findings.

We appreciate the thoroughness of the assessment of the scientific data underlying the effects of food components on health by EFSA and accept that the EFSA work is setting the boundaries of the beneficial nutritional and physiologic effects of food and food components on health. We would like to observe that these boundaries may serve as a useful addition to the established case law of the European Court of Justice on how to differentiate physiological from therapeutic effects. We understand that this is an important issue, in particular in relation to botanicals and we would like to offer our assistance in the current reflections of the European Commission.

Nevertheless, we remain concerned about the high number of unfavourable opinions/rejections relating to claims on other substances, despite the fact that we acknowledge that the evidence submitted for many of the claims in the Article 13 process is poor, in particular for submissions that were not part of the industry concerted action.

We see three further major reasons for these unfavourable opinions:

- Some rejections are a direct consequence of the discrepancy between the way in which the information has been compiled and presented and the way in which EFSA is carrying out its assessments. This is often leading to rejections of the scientific justification because of formalistic reasons. This is illustrated with a number of examples in the annex to this letter.
- Some rejections are caused by the almost exclusive reliance on randomised controlled trials demonstrating measurable and meaningful improvements of health (also called the pharmaceutical approach). We observe that this approach adopted by EFSA, has a number of weaknesses that prevent the recognition of the importance for health of many food components. These weaknesses include the focus on isolated food components (which often do not exist in isolation) rather than on foods, the expectation to provide evidence demonstrating improvement rather than maintenance of physiological functions, and the fact that the approach is biased towards effects on reductions of disease risk factors while leaving many more general health effects unaddressed. We feel that in many cases a full consideration of the totality of the evidence and an approach based on nutritional science would be able to arrive at more differentiated conclusions as a basis for the possible acceptance of certain claims.
- Finally, some rejections are caused by the way the claims legislation is being interpreted and we have reasons to believe that these interpretations are unduly restrictive and lead to the impossibility to acknowledge and assess a number of health effects under the terms of the claims legislation.

Given the importance of claims approvals, we believe these reasons for rejection need to be addressed. In particular a proper appreciation of the specificities and limitations of nutritional research is needed. We are observing a mounting concern by the scientific community, which may ultimately affect the credibility of the European system.

We would therefore ask the European Commission not to pursue with claims rejections based on the EFSA opinions that are currently available but to allow for a fundamental discussion of the points raised and a concurrent reappraisal of the process. Since the Article 13 process resides under the terms of reference of the EC, we would appeal to the EC to undertake this activity before proceeding with any decisions to reject claims.

In particular, we would suggest and support the following measures that may help provide more clarity on the validity of the individual rejected claims:

- Not to take decisions to prohibit claims on the basis of these EFSA opinions but allowed that these claims are resubmitted for evaluation in the same way as this is intended to be allowed for insufficiently characterised probiotics and insufficient claims.

- For such resubmission, accept that the procedure of Article 13.4 is appropriate and not to adopt a systematic obligation to submit a dossier under the Article 13.5 procedure.
- To address the problems with the scientific approach raised in this paper and enable discussions with EFSA on alternative approaches to consider the totality of the evidence and weigh the evidence to provide a balanced view on the strength, consistency and plausibility of health benefits of food components. Such alternative systems are used by other organisations and have also been explained in the claims model we developed.
- To involve in these discussions and on specific topics the views of academic experts in the field to achieve a consensus based acceptance of the health effects under consideration.
- To consider that claims that received a negative opinion because of the lack of characterization of the substance cannot be considered as claims to be included in the register of rejected claims. Likewise, that claims that are rejected because the health effects are considered general and non-specific should not be included in the register given that the NHCR explicitly allows such claims to be made if accompanied by an approved claim.
- To resolve the current vagueness and lack of clarity on the interpretation of what is accepted as a sufficiently characterised food or food components or a sufficiently specific health effect and what is not.
- To consider claims such as ‘*contains antioxidants, probiotics, etc*’, being interpreted as health claims but having no chance of being accepted under the EFSA assessment, as well understood generic descriptor of a group of ingredients, which could be addressed through the application of Article 1.4 of the NHCR or alternatively by an adaptation of the EC guidance document of 14 December 2007.

It has now been widely recognised that the implementation of the EU claims legislation is a learning process and that consequences only become fully clear as the process progresses. We provide this analysis in a constructive spirit to help the EC, the Member States and EFSA to understand issues that are related with the approach. And we offer our contribution in helping to resolve these issues as much as we can.

With kind regards,

EHPM – ERNA – EBF

Annex

Annex: Detailed comments in relation to the third batch of EFSA opinions

Introduction

These comments should be read in conjunction with the comments we have submitted in relation to the first¹ and second² batches of EFSA opinions that remain valid and are not repeated here.

We highly appreciate that the EC has considered many of these comments in a serious and professional way and also the openness with which we have been able to discuss them. This has led to the identification of a number of problems and to potential solutions, in particular relating to insufficiently characterised or substantiated claims and to botanicals. They have however not led to the fundamental reappraisal of the process for claims assessment that we feel is necessary.

In this annex we focus in particular on the third batch of opinions and its relationship with the assessment process, the terms of reference and the information on the EFSA approach that has come from further guidance and stakeholder meetings. The comments illustrate that a number of EFSA rejections are the direct consequence of the chosen approach for the assessment of the scientific evidence.

We already identified in our previous comments a number of elements that have led to the rejection of claims:

- The fact that no guidance was available on the correct characterisation of the substances, which led EFSA to reject many submissions without assessing the evidence.
- The fact that traditional use is not considered as part of the evidence to substantiate health effects for botanicals.
- The fact that studies in patients are largely not considered as part of the evidence in support of health effects relating to the maintenance of health.
- The fact that mainly claims where the evidence has shown to reduce or affect a risk factor for a disease state are accepted, both for Article 13.1, Article 13.5 and Article 14 claims.

We are grateful that some of these elements have been considered and are currently part of reflections that may readjust the process.

We would like to add in our current comments four additional elements:

¹ Joint ERNA-EHPM-EBF comments in relation to the first batch of article 13.1 claims opinions. Letter sent to the EC on 15 October 2009. <http://www.erna.org/UserFiles/HC%20Position%20EHPM-ERNA-EBF.pdf>

² Joint ERNA-EHPM-EBF comments in relation to the second batch of article 13.1 claims opinions. Letter sent to the EC on 15 May 2010. <http://www.erna.org/userfiles/file/HC%20comments%20nd%20batch%20EHPM-ERNA-EBF.pdf>

- The fundamental discrepancy between the format that was used to submit claims and the format adopted by EFSA to assess claims has led to information being presented in ways that are not accepted by EFSA.
- The fact that in the EFSA assessment and opinions there is no visible consideration of existing consensus and views or opinions of leading experts in the various research fields, resulting in a need to readjust EFSA opinions where necessary.
- The fact that the claims legislation itself and a number of its interpretations have hampered the possibility to address a number of health benefits.
- The fact that it is almost impossible to get claims approved for foods and combinations of food components, as the assessment is focussed on well characterised substances, isolated from the natural carriers and investigated in isolation or on artificial dietary interventions.

We strongly believe that these elements contribute to a number of rejections and that such is not justified.

1. Overview of claims covered thus far.

In the next sections we will elaborate on the elements raised above. But we would first like to present an overview of the claims assessed so far in relation to our joint CIAA-EBF-EHPM-ERNA submission. It is clear that statistics on numbers of rejections are biased because of the important number of claims that have been submitted in parallel with our concerted action. We cannot vouch for the quality of the submissions that have not been part of the industry exercise and we regret to see from the information in several EFSA opinions, that an important number of these submissions were of poor quality.

3rd batch

In the 3rd batch of opinions, we observe that 104 of our industry list claims are covered.

32 of these received a positive opinion (2 had already been assessed in previous batches, so this covers 30 new relationships). It covers mainly vitamins and minerals, but also some other substances: e.g. DHA, glucomannan, phytosterols and sterols/stanols.

47 of our industry list claims received a negative opinion. This concerns mainly other substances (e.g. CLA, CoQ10) and botanicals.

25 of our industry list claims received an inconclusive opinion for various reasons:

- 10 food constituents are insufficiently characterised (e.g. dietary fibre, whole grain foods, diet rich in whole grain/fibre and phosphatidylserine).
- In 1 case the evidence provided was deemed insufficient to establish a cause-effect relationship (cocoa flavanols & vascular health (ID 1507)).
- For 14 claims, the claimed effect was judged to be general and/or non-specific, outside of the scope of Article 13.1 (e.g. nutrition claim, children claim etc.) or non-complying with the NHCR for various reasons.

It is interesting to note that again no single claim relating to botanicals, probiotics or anti-

oxidants (except vitamin E as an essential nutrient) has received a positive opinion.

All batches compiled

If all three batches are taken together, we can draw the following conclusions:

As EFSA indicates, the opinions published in these three batches cover 1,745 claims from the list of 4,637. They cover 289 of the 776 claims included in the industry list (37 %).

Of these 289:

- 115 opinions have been positive (40%). These relate for the vast majority to vitamins and minerals (93 in total) and for the rest mainly to essential fatty acids and claims relating to blood lipids.
- 174 opinions have been negative (60%), of which 5 judged as insufficient and 47 covering insufficiently characterised probiotics. 44 claims related to botanicals (all negative).

Table 1 represents an overview of the outcome. For the classification we refer to the list as submitted³.

Table 1: Overview of the outcome of the three EFSA series of opinions on the submissions of the industry concerted list of Article 13.1 claims.

	Number of opinions	Positive	Negative	Insufficient	Insufficiently characterised
Vitamins	55	50	4	1	0
Minerals	47	42	5	0	0
Protein	4	2	2	0	0
Carbohydrates	6	0	6	0	0
Fat	12	5	7	0	0
Fibres	7	4	3	0	0
Probiotics	55	0	8	0	47
Foods	11	5	6	0	0
Diets	3	0	3	0	0
Others	45	7	34	4	0
Botanicals	44	0	44	0	0
Total	289	115	122	5	47

2. Discrepancy between the information submitted and the expectations for the assessment

2.1. Requirements of Article 13

We note from the EFSA press release accompanying the publication of the 75 opinions of the 3rd batch that:

³ Joint CIAA-EBF-EHPM-ERNA submission for the list of article 13 claims. <http://www.erna.org/Industry-article-13-list.aspx>

“As for EFSA’s previous work on ‘general function’ health claims, scientific experts on EFSA’s NDA Panel issued unfavourable opinions on many of the claims in this series due to the poor quality of the information provided to EFSA. Information gaps included for instance: inability to identify the specific substance on which the claim is based (e.g. claims on “dietary fibre” without specifying the particular fibre); lack of evidence that the claimed effect is indeed beneficial to the maintenance or improvement of body functions (e.g. claims on renal “water elimination”); lack of precision regarding the health claim being made (e.g. claims referring to terms such as “energy” and “vitality”); or lack of human studies with reliable measures of the claimed health benefit.”

We regret that such communication from EFSA conveys to the public a message that the information provided by the European industry is of poor quality, while much of it is in fact the result of the process and the mismatch of what has been provided with expectations that only later became clear.

In 2006, when the sector federations joined forces and started work on the compilation of their contribution to the Article 13 list there was no guidance on how this Article 13 list should be compiled, nor was there information relating to the type and nature of the information EFSA would require.

The joint industry list (elaborated by CIAA-EBF-EHPM-ERNA) covers 776 substances-health relationships. For these claims a defined methodology was followed. This methodology was developed, in the absence of official guidance, to the best knowledge of independent experts that have also assessed the submissions for their inclusion and was published as a guideline⁴. The methodology and accompanying template for the submission of evidence have been presented to the Member States and has largely been the basis for them to accept submissions. We observe that a number of requirements, recommended in the guideline has now appeared to be fundamentally different from the expectations of EFSA and therefore a number of claims has been judged not acceptable and others have been rejected because the information was not appropriate to warrant a positive assessment.

We believe this is a serious issue that would need to lead to an opportunity to correct the information submitted for a number of claims in addition to the insufficient and insufficiently characterised ones currently under discussion.

The guidelines clearly took a broader view than EFSA on the possible health effects and have presumed a different approach, focussing on an assessment of the totality of the available data to support health effects, also in the absence of randomised controlled trials (RCTs). The guidelines (to our judgement still correctly) assumed that for generally accepted claims under Article 13.1 of the Regulation, a full scientific dossier was not required. This was not disputed at any time and has not been requested by any Member State during the compilation of the list. However, this unavoidably means that the information cannot be as complete, as is the case with an application for authorisation under Article 13.5 or Article 14, for which EFSA has issued a 42-page guidance with extensive templates.

⁴ Richardson DP, Binns NM, Viner P. (2007) Guidelines for an evidence-based review system for the scientific justification of diet and health relationships under Article 13 of the new European legislation on nutrition and health claims. Food Science and Technology Bulletin: Functional Foods 3 (8) 81–95.

Only after the claims had been submitted it became clear that EFSA expects the same information and applies the same assessment approach as for an application for authorisation⁵. We believe this is not appropriate and not in line with the proportionality of the NHCR that foresaw three different procedures, the Article 13.1 one as the least demanding.

We understand that the EC and Member States are still discussing the way for the submission of additional data for insufficient claims and insufficiently characterised probiotics, either to proceed via an Article 13.5 submission or via the Article 13.4 process. As there is no requirement for the submission of a dossier for article 13.1 submissions, this should also not be the case for the submission of further information. We feel that a systematic obligation to use the Article 13.5 procedure is not justified, not only because of its requirement to submit an application under the form of a dossier, but also because the information to be submitted in many cases would not fit under its scope. It is obvious that any applicant is always entitled to submit an application under Article 13.5 based on new data if it wishes to do so.

We would therefore ask to the EC, in particular in the interest of SMEs to give due consideration to the possibility of Article 13.4 for the modification and the submission of additional information to entries of the list.

2.2. Claims falling out of the scope of article 13.1

We have noted that EFSA has not considered the evidence submitted for a number of claims because it is of the opinion that the claims submitted do not fall under the scope of article 13.1. This is the case where EFSA has considered that the substance of the claimed effect is not sufficiently characterised, that the claimed effect is general and non-specific, that the claim relates to improved bioavailability or because the claim is considered to fall under the scope of article 14. The first two instances are covered more extensively in points 2.3 and 2.4 below.

In the bioavailability opinion⁶, EFSA considers that the claimed effects refer to the improved bioavailability of a nutrient rather than to a relationship between a food/food constituent and health and therefore falls out of the scope of Article 13.1. In the same opinion EFSA considers that a number of claims refers to beneficial nutritional properties of a food/food constituent, which makes them fall out of the scope also. It should be noted that such interpretations should be considered with care and that such claims cannot systematically be considered as not being health claims. The lack of guidance has made Member States accept such claims as Article 13 claims and by not accepting these for assessment, EFSA prejudices their legal status and subsequent transition periods. It is not clear what measures the EC and the Member States will envisage relating to such claims.

⁵ EFSA Briefing document for Member States and European Commission on the evaluation of Article 13.1 health claims. EFSA Journal 2009; 7(11):1386. <http://www.efsa.europa.eu/en/efsajournal/pub/1386.htm>

⁶ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and improved bioavailability of nutrients (ID 384, 1728, 1752, 1755), energy and nutrient supply (ID 403, 413, 457, 487, 667, 1675, 1710, 2901, 4496) and presence of a nutrient in the human body (ID 720) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1743

The many claims that EFSA has not considered because they are judged to fall under article 14 (mainly children's development and health claims), is also of concern. As a general comment we consider that it is not within EFSA's competence to judge under what article or definition a certain claim falls, when these claims have been submitted by the Member States and the EC under article 13 (and in particular since EFSA has indicated that the same criteria for assessment will apply to all claims irrespectively). We consider that the EC expects guidance from EFSA on whether the scientific substantiation provided would only be valid for children. However, the general principle is that claims that are valid for the general population, including children, would need to be considered as article 13.1 claims, be assessed as such and be permitted in case of a positive opinion on all products, including products that may also be consumed by children. We would like to ask the EC to safeguard this principle, clearly stated in the 14 December 2007 interpretation note⁷ and avoid that general claims that are approved would need to be reintroduced under article 14 to accept their use also on products that are consumed by children.

In its children opinion⁸, EFSA assumes that claimed effects including "fetal growth", "neural tube development", "neurological development in embryos", "growth and development and maintenance", "brain development in the foetus", etc refer solely to children's development and health and therefore fall out of the scope of article 13.1. We would like to note that this is an interpretation and that such claims may also be considered to relate to pregnant women. When the article 13.1 list was being compiled, no clarity existed on this and as a consequence, such claims have been included and accepted by the Member States. Excluding these at this point is not appropriate and has consequences for the legal status and the transition periods applicable.

In view of the above, we would ask the EC to consider that all claims are assessed on the merit of the evidence submitted and not be excluded on the basis of discussions or interpretations that have developed in the course of the process.

2.3. Discrepancies affecting the characterisation of the food or food component

Below are examples of the main discrepancies between the different methodologies observed that have lead to the rejection of potentially valuable health effects. These elements could and should be modified to enable the full spectrum of health effects of foods and food components to be recognised. These elements include:

Our guidance considered that the food, category of foods or food component, subject to the claimed effect, should be sufficiently characterised. This means that information on the characterisation of the substance or food needs only to be as detailed as is pertinent to the

⁷ Guidance on the implementation of Regulation n° 1924/2006 on Nutrition and health claims made on foods. Conclusions of the standing committee on the food chain and animal health. 14 December 2007 http://ec.europa.eu/food/food/labellingnutrition/claims/guidance_claim_14-12-07.pdf

⁸ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) that are referring to children's development and health (ID 38, 110, 257, 490, 542, 623, 1896, 2898) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1731

beneficial effect. This makes it possible to introduce claims for groups of substances, foods or diets that share a common characteristic or for groups of substances sharing similar effects. It is clear that the Member States and the EC have accepted this as valid subjects of Article 13.1 claims.

However, since EFSA considers characterisation in an absolute way and only considers studies performed with individual substances or foods with well defined amounts of those substances as pertinent, generally accepted claims for e.g. dietary fibre, are not considered eligible. Furthermore, in some cases the characterisation of the substance is interpreted by EFSA and does not cover what was originally the scope of the submission.

Below are some examples of problems associated to the characterisation, taken from EFSA opinions:

The process is not able to reach positive conclusions on complex foods or mixtures of food components because of the lack of characterisation

- **Dietary Fibre⁹**: In its opinion on dietary fibre, EFSA considered that dietary fibre is the common name for all carbohydrate components occurring in foods that are non-digestible in the human small intestine. These components include non-starch polysaccharides, resistant starch, resistant oligosaccharides with three or more monomeric units, and other non-digestible, but quantitatively minor, components when naturally associated with dietary fibre polysaccharides, especially lignin. However, it does not consider dietary fibre to be sufficiently characterised in relation to the claimed effects covered by the opinion, mainly because different fractions can have different effects, which is obviously correct.

However, the result of this approach is that no claim for dietary fibre as such can be accepted under the approach adopted by EFSA, whereas beneficial effects associated to an increase of dietary fibre in the diet are part of most, if not all nutritional recommendations and would therefore be useful also to be communicated on products that can contribute significantly to fibre intake.

The World Health Organization/Food and Agriculture Organization (WHO/FAO) report of 2003 on Diet, Nutrition and the Prevention of Chronic Diseases¹⁰, submitted as part of the evidence, concluded that the available evidence for an effect of dietary fibre on body weight regulation and the prevention of obesity was convincing based on epidemiological evidence and the results from two meta-analyses of randomised controlled trials (RCT) assessing the effects of mixed, “soluble” and “insoluble” types of fibre on body weight compared to low-fibre diets both ad libitum and during energy restriction. This report further indicates that increased intake of dietary fibre has a probable beneficial effect on the reduction of type 2 diabetes and cardio-vascular disease. It is therefore not defensible that EFSA cannot reach conclusions on such important effects for public health.

⁹ Scientific Opinion on the substantiation of health claims related to dietary fibre (ID 744, 745, 746, 748, 749, 753, 803, 810, 855, 1415, 1416, 4308, 4330) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 EFSA Journal 2010;8(10):1735

¹⁰ World Health Organization/Food and Agriculture Organization (WHO/FAO) 2002. Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series 916

- **Whole grain¹¹**: The same holds true for whole grain, covering an equally important recommendation for public health that is not considered because of the difficulty of EFSA to characterise what whole grain is.

We believe that a system that is not capable to arrive at positive conclusions on the generally accepted health effects of dietary fibre and whole grain has considerable weaknesses and calls for a review. After all, how credible will be the EU system if on the basis of this opinion the following claims would be included in its register of refused claims:

- Dietary fibre helps to maintain normal bowel/colonic function
- Diets high in fibre help control your weight.
- Foods high in fibre help you to feel full for longer to help maintain your body weight
- People who eat foods high in fibre tend to have a healthy heart.
- Whole grain promote bowel function/helps to maintain normal bowel function

We have maintained that claims should be assessed by looking at the totality and weighing of the evidence and have proposed and supported a system that grades the evidence to enable the EC and the Member States to take decision, well informed of the strength, consistency and plausibility of the effect. An opinion that concludes that dietary fibre is not sufficiently characterised and that therefore a cause and effect relationship cannot be established does not provide sufficient information to base decisions on.

The strong focus on well-defined substance characterisation leads EFSA to consider much of the observational studies that have been performed with the foods as such as not pertinent for the assessment of the claims.

- **Protein¹²**: In its protein opinion, EFSA considers that protein is well characterised (as opposed to dietary fibre). Also in this case it is well known there are different proteins with different actions and in particular the protein quality may vary considerably between various sources. Nevertheless in this case characterization was deemed sufficient and claims have been assessed. But we observe that only those claims that were based on consensus opinions/reports from authoritative bodies and reviews that showed that there is good consensus on the role of dietary protein and the respective function received positive opinions.
- **Soy Protein¹³**: In its soy protein opinion, EFSA took another view. It acknowledges that food products containing soy protein usually also contain variable amounts and types of phenolic

¹¹ Scientific Opinion on the substantiation of health claims related to whole grain (ID 831, 832, 833, 1126, 1268, 1269, 1270, 1271, 1431) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 EFSA Journal 2010;8(10):1766

¹² Scientific Opinion on the substantiation of health claims related to protein and increase in satiety leading to a reduction in energy intake (ID 414, 616, 730), contribution to the maintenance or achievement of a normal body weight (ID 414, 616, 730), maintenance of normal bone (ID 416) and growth or maintenance of muscle mass (ID 415, 417, 593, 594, 595, 715) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1811

¹³ Scientific Opinion on the substantiation of health claims related to soy protein and contribution to the maintenance or achievement of a normal body weight (ID 598), maintenance of normal blood cholesterol concentrations (ID 556) and protection of DNA, proteins and lipids from oxidative damage (ID 435) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1812

compounds, such as isoflavones, and variable amounts of fatty acids and fibre, which could contribute to the claimed effects. EFSA therefore focussed its assessment on the protein component in soy, since neither the food constituent nor the conditions of use for these claims provided consistent specifications regarding other components in soy besides protein. This approach is theoretic and ignores that soy protein does not occur in the diet as such. Furthermore, as it is not part of the diet in isolation, it is also not as such subject of intervention trials in support of health effects. It is therefore not surprising that EFSA could not draw conclusions for the scientific substantiation of the claimed effect because the scientific evidence does not allow one to distinguish between the effects of the protein component of soy (which is the subject of the health claim) and those of soy isoflavones on lipid peroxidation. This clearly shows the problem with the approach. There may therefore be a case for reconsidering the characterisation of the food and either allow for the submission of further clarification or for a review of the conclusions by EFSA by focussing on a broader definition of ‘soy protein’ that is more in line with reality.

- **Tea¹⁴**: In its opinion on tea and tea catechins, EFSA considers that *Camellia sinensis* (L.) Kuntze (tea) is not sufficiently characterised in relation to the claimed effects, but catechins from green tea (including EGCG) are. It bases its assessment on the fact that the composition of the tea leaves depends on a variety of factors, including climate, season, horticultural practices, and the type and age of the plant and that many kinds of tea are produced (which can be classified into three major types according to the different degrees of fermentation: green (un-fermented), oolong (semi-fermented) and black (fully fermented)). It goes on to say that the composition of tea beverages greatly depends on the type of leaves used, on the degree of fermentation and on the methods of preparation. The degree of fermentation, the production process and the method of preparing the tea infusion have not been described in relation to the claims. It is clear that such an approach considerably limits the possibility to have claims for tea as such accepted and one can wonder if this is an appropriate application of the NHCR.

These examples illustrate the difficulty that exists to have a claim approved for a food as such. The characterisation expected requires standardisation of the food (in this case tea or tea extract, for the active compound present, in this case catechins). The assessment process therefore favours claims that are valid for substances isolated out of their natural carrier foods (or for foods that are standardised in relation to such active components). This is because most observational food studies do not characterise foods and therefore are rejected as pertinent for the claimed effect. In many cases, EFSA only accepts health benefits if they have been investigated on well defined food components. And in doing so, EFSA often does not consider studies that involve the natural food containing the substance because of its variable content or because the effects of the substances cannot be distinguished from other components contained in the food. This is another element that could be corrected if the totality of the evidence is judged in a different way and if claims would be based on the foods and food components that are actually consumed.

¹⁴ Scientific Opinion on the substantiation of health claims related to *Camellia sinensis* (L.) Kuntze (tea), including catechins from green tea, and contribution to the maintenance or achievement of a normal body weight (ID 1107, 1112, 1544, 2716), increased beta-oxidation of fatty acids leading to a reduction in body fat mass (ID 1123, 1124, 3698), and maintenance of normal blood glucose concentrations (ID 1115, 1545) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1791

The strong focus on pure food components makes it difficult to accept natural variability associated with the composition of foodstuffs.

- **Pomegranate¹⁵**: EFSA has addressed a number of opinions relating to specific fruits and vegetables. In one, taken as an example, EFSA has grouped claims relating to pomegranate/pomegranate juice and polyphenols contained therein and considered that pomegranate, its juice and even the polyphenols are not sufficiently characterised and only punicalagin and ellagic acid are. Consequently, EFSA rejects the value of studies in which pomegranate/pomegranate juice has not been characterised with respect to its polyphenols (i.e. punicalagin and/or ellagic acid) and retains only few studies as pertinent. We feel this is not addressing the subject of the submission, which is the fruit and its juice. It does also not reflect the reality where not the pure compounds but the natural fruit is eaten and obviously, studies performed with the pure compounds would only be relevant in the case of the use of these substances as such.
- **Propolis¹⁶**: In its propolis opinion, EFSA considers that the type and content of flavonoids in propolis may vary depending on the specific propolis raw material as well as the extraction and preparation methods, and that flavonoid-free propolis has been reported in the literature. Differences were observed in the qualitative and quantitative values of constituents in the propolis from various geographical origins. For these reasons, propolis could not be sufficiently characterised and the scientific evidence underlying the claimed effects was not considered.

It is not appropriate that variation in specific “active” substances or compounds naturally contained in a food leads to the rejection of claims due to insufficient characterisation, as it is not possible to consider or include all forms and types of a natural raw material. What was expected from EFSA was to assess the evidence submitted and provide clarification on what effects are justified and under what conditions. Where appropriate, this assessment could lead to specifications or conditions of use (e.g. identifying an minimum content of flavonoids). However, for foods, it is unavoidable that the natural variability in composition is accepted and considered. It is not possible nor intended that for all different products marketed a specific application is submitted. But based on the literature, a common condition of use can often be established that would be a benchmark for the whole category of food and would also take into consideration the natural variation of such natural products.

The strong focus on well-characterised food components favours effects that can be demonstrated by interventions with substances on top of the normal diet but largely fails to assess beneficial effects of modifications of the diet itself.

- **Hydroxypropylmethylcellulose (HPMC)¹⁷ and Pectin¹⁸**: In these opinions, EFSA accepts that

¹⁵ Scientific Opinion on the substantiation of health claims related to pomegranate/pomegranate juice and maintenance of normal blood cholesterol concentrations (ID 1162, 1320, 2107, 2167), maintenance of normal erectile function (ID 1163), protection of lipids from oxidative damage (ID 1201, 1319, 2123), “antioxidant and anti-aging properties” (ID 1901), increase in appetite after unintentional weight loss leading to an increase in energy intake (ID 2122) and maintenance of normal blood glucose concentrations (ID 4471) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1750

¹⁶ Scientific Opinion on the substantiation of health claims related to propolis (ID 1242, 1245, 1246, 1247, 1248, 3184) and flavonoids in propolis (ID 1244, 1644, 1645, 3526, 3527, 3798, 3799) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1810

¹⁷ Scientific Opinion on the substantiation of health claims related to hydroxypropyl methylcellulose (HPMC)

the addition of 4 g of HPMC and at least 10 g of Pectin respectively have been shown to reduce post-prandial glycaemic responses.

In contrast, in its glycaemic index opinion¹⁹, EFSA comes to the conclusion that carbohydrates that induce a low/reduced glycaemic response and carbohydrates with a low glycaemic index (e.g. <55) are not sufficiently characterised. This is mainly because post-prandial glycaemic responses to different carbohydrates depend on the chemical and physical properties of the particular type of carbohydrate being considered as well as on individual factors (i.e. the extent to which foods are chewed prior to swallowing, biological variation in rates and extent of digestion and absorption) and the glycaemic index of a carbohydrate-containing food also depends on several factors other than the amount of available (glycaemic) carbohydrates present (e.g. amount and type of dietary fibre, amount of dietary fat, energy density, physical properties, mode of preparation).

So although EFSA considers that reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect, it is not able to assess such effects for naturally occurring carbohydrates in the diet, because of its reliance on RCTs carried out with interventions with well-characterised substances. This is at contrast to effects of indigestible substances that are added to the diet, often in high amounts (e.g. pectin and HMPC), since the addition of such compounds can be controlled and the effects assessed in intervention trials. This again shows that the approach is not suitable to cover all aspects of nutritional research. One could wonder if the failure to assess effects of normal constituents of the diet as compared to additional intake of substances is justified.

We also observe that EFSA has difficulties in assessing claims relating to the presence of macronutrients in the diet. It is clear that effects of changes in one macronutrient fraction (e.g. protein, fat or carbohydrates) are not assessable under the current approach because of the fact that any increase of a macronutrient is compensated by a decrease in another and vice versa. And any modification that is not compensated results in a decrease or increase of the energy value.

- **Protein**¹²: In its protein opinion, EFSA considers that the studies provided do not allow conclusions to be drawn about the role of protein per se (i.e. independently of other dietary manipulations) on body weight control because the intervention and control diets prescribed differed in aspects other than the protein content, which could have an impact on body weight changes. It is impossible to vary dietary protein, carbohydrate and fat content independently of one another using a single control pre-load.

Obviously studies on effects of macronutrients will always involve changes in the composition of fat and carbohydrates. Furthermore, individual effects of protein can only be

and maintenance of normal bowel function (ID 812), reduction of post-prandial glycaemic responses (ID 814), maintenance of normal blood cholesterol concentrations (ID 815) and increase in satiety leading to a reduction in energy intake (ID 2933) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1739

¹⁸ Scientific Opinion on the substantiation of health claims related to pectins and reduction of post-prandial glycaemic responses (ID 786), maintenance of normal blood cholesterol concentrations (ID 818) and increase in satiety leading to a reduction in energy intake (ID 4692) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1747

¹⁹ Scientific Opinion on the substantiation of health claims related to carbohydrates that induce low/reduced glycaemic responses (ID 474, 475, 483, 484) and carbohydrates with a low glycaemic index (ID 480, 481, 482, 1300) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010; 8(2):1491

shown with controlled protein supplementations, a completely unnatural situation. In its linoleic acid²⁰ opinion in the first batch of Article 13 opinions, EFSA accepted the beneficial role of linoleic acid relating to the maintenance of normal cholesterol concentrations mainly because of the results of a meta-analysis of controlled clinical trials showing that replacing 1% of energy from carbohydrates with PUFA reduced LDL-cholesterol concentrations by 0.02 mmol/L. But such intervention trials necessitate conditions that are not likely to occur in the normal diet. This is another weakness of the reliance on RCTs to substantiate health effects for foods. It does not work with the diet as it is and is not capable to address certain dietary changes. An alternative approach, considering the totality of the evidence may also be more suitable in this case. Guidance to learn about what study designs would be acceptable would be welcomed also.

Conditions for the claim to be valid

From our guidance, it was very clear that it would be necessary to state, wherever appropriate, the quantity of the food or food component that will produce the nutritional or physiological effect claimed, or perhaps the amount that should be consumed per quantified serving or per day as a condition of use. We even considered it might be necessary in certain cases to indicate the pattern of consumption needed to achieve the claimed health benefit, to indicate if the health relationship applies only to certain groups of the population or if the food should not be used by certain groups.

But since the list was not intended to cover each and every different form and carrier of a substance, we also allowed for more generally phrased conditions of use. In particular for botanicals, we accompanied our submission with a specific explanatory note in this respect.²¹ As already highlighted in the chapter on characterisation above and illustrated by the example of tea, this is not always considered as such.

We understand that well-characterised substances or products are the best way for assessing the pertinence of specific intervention trials. However, we feel this is not always necessary and certainly not within the scope of the Article 13 list. If this were a requirement or the law, it would mean that every single manufactured functional ingredient would need to figure in the list, as every company uses different processing methods and thus final products always differ. This is in particular the case with extracts and isolates, the composition of which can vary widely. Submitting claims for every single one would result in a multiple of the current number of submissions. We therefore looked for a way to express conditions of use that would be applicable to many products of the same nature, sharing the same compound or characteristic. Complementary, companies with very defined substances and own research could apply for a claim under Article 13.5 and benefit from data protection.

In most cases the claims made on products relate to the functional components included in its composition and its activities described in scientific literature. This makes it possible to use

²⁰ Scientific Opinion on the substantiation of health claims related to linoleic acid and maintenance of normal blood cholesterol concentrations (ID 489) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 on request from the European Commission. EFSA Journal 2009; 7(9):1276

²¹ Accompanying note on conditions of use for botanicals.

<http://www.erna.org/UserFiles/File/art13%20ERNA/Acomp%20note%20on%20COU.pdf>

these components as functional markers of product composition and avoid the need for submission of all individual products or food ingredients. It was our legitimate expectation that EFSA would look at all the available evidence to establish what the scope and conditions of use would be for a claimed effect, including where appropriate the amount of the functional marker. EFSA first identifies the substance and then only looks at the evidence directly related to that substance. This is in our view a too restrictive approach.

Also the conditions of use are set in a very pragmatic way for vitamins and minerals, i.e. as a fraction of RDA. We regret that this methodology is only applied to essential nutrients and not to other non-essential food components that are judged to be beneficial for health.

Conclusion

The approach of EFSA relating to characterisation and accepting only substances (and evidence from substances) that are well defined, is in our view not appropriate as all foods and food components should be eligible for making appropriate claims. It leads to a situation where it is very difficult to have claims for normal foods (or its active components) approved as all evidence based on insufficiently characterized food is rejected. EFSA considers that characterisation is a scientific judgment. This implies that if the characterisation is not accepted, the scientific evidence is not considered and the claim is rejected.

The EC has accepted that probiotics that had not been characterised according to guidelines issued later by EFSA, should benefit from an opportunity to complete or add such characterisation. However, EFSA has not published guidance for other substances, e.g. foods or botanicals. In order to avoid discrimination between claims, we would ask that all claims that are rejected by EFSA for the same reason (i.e. insufficient characterisation) should benefit from the same possibility.

Furthermore, a system that starts from an assessment of the information on the substance-health relationship, considering all possible forms of the food/food component and not exclusively from a predetermined well characterised isolated substance and derives its conclusions from an assessment of the totality of the evidence, would be more suitable to address the complex interactions between foods and health. Such an approach is advocated in the claims model we developed²².

Finally, we would like to remark that characterisation is also affecting the status of the claim. When the food or food component cannot be characterised, the claim cannot fall under the scope of the NHCR, as there is no food or food component for the claim. Such claims can therefore not be rejected and put in the register of rejected claims.

²² ERNA. 2009. Model for the assessment of article 13.1 health claims in the framework of the EU nutrition and health claims regulation in relation to the terms of reference.
<http://www.erna.org/UserFiles/Claims%20Model%20Final.pdf>

2.4. Discrepancies affecting the characterisation of the health relationship

It is clear from our guidance document on Article 13 submissions that the health relationship under Article 13 must relate to the maintenance or enhancement of healthy body functions, organs of the body or health in general, and must refer only to the healthy state of those body functions or processes (body metabolism, cholesterol levels, metabolism, digestion etc.). The guidance indicated that the Article 13 list could cover claims indicating that for example nutrients and other substances could be necessary for and/or contribute to the structure and functions of particular organs and physiological states, such as reproduction, conception, growth and development, and body maintenance, all well-established functions of vitamins and minerals, and many other substances that are documented extensively in the scientific literature. Likewise, the Article 13 list could also cover claims for foods or food components relating to specific beneficial effects on physiological, psychological, cognitive functions or biological activities. Substances could be included in the Article 13 list as long as they have well-established physiological or biological functions in the body. For example, a function of a food or food component can apply to constituents that have effects on calcium-absorption, or cholesterol-lowering or prebiotic/probiotic effects. Specific physical or chemical properties of a food or food component may influence a particular physiological effect, e.g. a low glycaemic index due to specific structural or starch properties. Finally, it also accepted to cover specific diets that may have specific effects on health in general, in so far as the effect of such diets can be attributed to the foods, food components, nutrients or other substances that characterize the specific diet (e.g. high in fibre, low in fat etc.).

In our guidance we therefore took a very clear focus on the health relationship. Our decision to focus on the relationship rather than on very specific wordings was motivated by two reasons:

- Firstly, we considered that in the Article 13 list, not all individual claims for a substance would be included, but that its beneficial role for a specific health relationship would be acknowledged. We expected that EFSA would look at the totality of the information available/submitted and would indicate the scope and therefore boundaries of the health benefit.
- Secondly, it reflected current practice that many health claims made on products are of a general nature (though not necessarily vague or non-specific). They are formulated to let consumers understand that consumption of the food or its constituents are useful for the maintenance of specific physiologic functions, without specifying the exact mechanisms of action (which would be too technical for the consumer to understand).

For these reasons the Article 13 list template contained two columns: one with the health-relationship and one with example wordings. These wordings were intended to be examples of how the claim was made but not to serve as claims for the assessment. The guidance makes it clear that the wording in the template can only be an example and could not represent an exhaustive list of possible claims. However, it was stressed that the examples given are consistent with the health relationship and the nature of the supporting evidence, and do not imply benefits that go beyond the scope and strength of the evidence presented. It was thought that although the wording of specific claims should not be the focus of the scientific evaluation, an understanding of the potential or actual claims that the health relationship

might support would help define the relationship in question for the EFSA scientists.

Later in the process and after the claims had been submitted, it became clear that EFSA looks at very precisely defined claims, taken from the list of examples, to assess. We had expected that EFSA would look at the totality of the scientific references provided and assess from that evidence if it is sufficient to validate the health relationship, i.e. if the substance is helpful for the maintenance of the function or an organ in the body. We had not anticipated that EFSA would take individual statements and see if there are RCTs available that confirm a statistically significant improvement of the function.

Obviously therefore these two approaches are fundamentally incompatible and lead to the rejection of many of the claims because EFSA inevitably makes selective assumptions as to the scope of the claims. These assumptions may not have been intended and might in fact refer to a claim that is going beyond the scientific evidence. We feel that a consideration of the totality of the available evidence is needed to define generally accepted health benefits.

Below are some examples of problems associated to the characterisation of the claimed effect, taken from EFSA opinions:

Lack of acceptance of the health relationship as sufficiently characterised to be assessed is eliminating whole areas of health benefits from the scope of the NHCR

The lack of guidance and clarity of interpretation of what is accepted as a sufficiently specific health effect and what is not, is creating an environment of much insecurity. Even for obvious health effects the fate in the eyes of EFSA is not clear.

We would therefore welcome further guidance from EFSA to have clarity on the reasoning behind the opinions on a number of health effects. But we would also like to remark that all Article 13.1 submissions have been done in the absence of such guidance and that therefore a chance should be given to complement or clarify submissions in the light of new guidance that will become available. This is all the more important since in many cases, EFSA rejects health relationships because they are considered too vague or not well defined and the reasons underlying such judgments are not clear.

- **Calcium²³**: In its calcium opinion, *cell membrane permeability* is judged not sufficiently characterised and EFSA concludes that the claimed effect is general and non-specific and does not refer to any specific health claim as required by the Regulation.

²³ Scientific Opinion on the substantiation of health claims related to calcium and maintenance of normal bone and teeth (ID 2731, 3155, 4311, 4312, 4703), maintenance of normal hair and nails (ID 399, 3155), maintenance of normal blood LDL-cholesterol concentrations (ID 349, 1893), maintenance of normal blood HDL-cholesterol concentrations (ID 349, 1893), reduction in the severity of symptoms related to the premenstrual syndrome (ID 348, 1892), “cell membrane permeability” (ID 363), reduction of tiredness and fatigue (ID 232), contribution to normal psychological functions (ID 233), contribution to the maintenance or achievement of a normal body weight (ID 228, 229) and regulation of normal cell division and differentiation (ID 237) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1725

In the same opinion, EFSA considers that *reduction of tiredness and fatigue and contribution to normal psychological functions, which encompass cognitive and affective domains* are sufficiently characterised health effects and beneficial to health. It is difficult to see logic.

- **Immune function²⁴**: In an omnibus opinion a number of claims were summarized relating to maintenance of the immune system as expressed in wordings as *immune system, immunity, immune health, immune system function, immune system/exercise stress, natural defences, système immunitaire, stimule l'immunité, système immunitaire, immunostimulant, it improves the immune system and most biological function and support immune defences*. These claimed effects were judged not sufficiently defined and the evidence was not considered. This is in contrast to the Vitamin C opinion²⁵ where a claim on the maintenance of a normal immune function was accepted.
- **Digestive system²⁶**: The same holds true for the claims relating to the *maintenance of, or contribution to, a healthy and balanced digestive system*, which EFSA judges to be not sufficiently defined. Nevertheless this presents a very important area of health effects that is not considered simply because the health effects are not considered to be sufficiently defined.
- **Energy and vitality²⁷**: In its opinion relating to energy and vitality, EFSA considers that the claimed effects (*energy, energy and vitality, vitalizing*) are not sufficiently defined, are general and non-specific and do not refer to any specific health claim as required by Regulation. The same applies to claims relating to *invigoration of the body, rejuvenation, tonic, stimulant, etc.* Although we accept that such statements are not very specific, they are claims often used in relation to botanical products and thus well understood by the consumers. Such claims refer to physiological (energy metabolism, reduction of tiredness) or to psychological functions, both categories explicitly included in the scope of the Article 13.1 list. The fact that they have been allowed by the Member States to be submitted should therefore result in an assessment. It is not acceptable that these claims are not considered or even rejected based on interpretations that have

²⁴ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and “immune function/immune system” (ID 433, 605, 645, 791, 1384, 1451, 1624, 1743, 1776, 1838, 1851, 1854, 1891, 1895, 3074, 3191, 3211, 3218, 3336, 3341, 3450, 3514, 3658, 3756, 3802, 3805, 3841, 3935, 3979), “contribution to body defences against external agents” (ID 2344, 3208, 3213, 3270, 3278, 3285, 3294, 3309, 3387, 3424, 3428, 3536, 3537, 3539, 3575, 3577, 3579, 3582, 3603, 3618, 3755, 3776, 3777, 3778, 3801, 3804, 3840, 4367, 4472), reduction of inflammation (ID 1327, 1391) and decreasing potentially pathogenic gastro-intestinal microorganisms (ID 2362, 2730, 4064) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1799

²⁵ Scientific Opinion on the substantiation of health claims related to vitamin C and reduction of tiredness and fatigue (ID 139, 2622), contribution to normal psychological functions (ID 140), regeneration of the reduced form of vitamin E (ID 202), contribution to normal energy-yielding metabolism (ID 2334, 3196), maintenance of the normal function of the immune system (ID 4321) and protection of DNA, proteins and lipids from oxidative damage (ID 3331) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1815

²⁶ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) claiming “healthy and balanced digestive system” (ID 1371, 4228), increasing numbers of gastro-intestinal microorganisms (ID 864, 1371, 3073, 4228) and decreasing potentially pathogenic gastro-intestinal microorganisms (ID 864, 1371, 3073, 4228) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1767

²⁷ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and “energy and vitality” (ID 18, 26, 62, 105, 122, 145, 165, 3962, 4054, 4440), “invigoration of the body” (ID 2383, 2386, 2391, 2393, 2409, 2441, 2463, 2488, 3834, 3883), “general health” (ID 1313, 3348, 4182, 4613), “rejuvenation” (ID 3981, 4023), “tonic” (ID 1703, 3462, 3581, 4418), “stimulant” (ID 3190, 3506) and “metabolic benefits” (ID 4438) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1738

been delivered after the deadline for submission.

It may be difficult for EFSA to assess psychological effects on the basis of RCTs, but a rejection of such claims because they are not sufficiently specific is not an acceptable solution. We believe this discrepancy must be addressed from both sides (submitter and assessor) and clarification needs to be provided on the requirements for the substantiation of claims relating to psychological and behavioural functions. If it would appear that the claims mentioned above are not considered as health claims, they should not be included in the register of rejected claims.

- Biotransformation of xenobiotic substances**²⁸: In its opinion on biotransformation of xenobiotic substances, EFSA has considered that terms such as *purification, purifying/detoxifying, urinary elimination, depurative, detoxificant, detoxification, blood health, supports the natural mechanism for body's purification, elimination and detox,* and *favours toxin elimination* refer to biotransformation of xenobiotic substances, but that it has not been clarified xenobiotic substance or which biotransformation reaction related to the elimination of xenobiotic substances is the target for the claim. It therefore considers that the claimed effect is general and non-specific and does not refer to any specific health claim as required by the NHRC.

We would not agree with that interpretation. Such terminology is often used on botanical products, typically to indicate support of the well-recognised physiological role of liver and kidneys to detoxify and excrete metabolic waste products and toxic substances. This represents a general function and is not necessarily substance specific. It may therefore also be difficult for EFSA to link such function to RCTs and specific measurable effects, but the detoxification role of liver and kidneys are normal physiological functions that should be considered valid as the subject of a health claim.

Furthermore, we have noted in the selenium opinion²⁹ that EFSA has interpreted “detoxification” as relating to the protection against heavy metals and has considered this as a beneficial physiological effect. Also, in another selenium opinion³⁰ from the first batch, EFSA stated that “Selenoproteins have a number of functions, comprising various catalytic roles (glutathione peroxidases, thioredoxin reductases, and iodothyronine deiodinases), structural roles, detoxifying functions (e.g. selenoprotein P) and storage and transport activities.” It is therefore not very consistent to consider detoxifying functions as beneficial for essential nutrients, but too vague for non-essential food components.
- Antioxidants**³¹: In its antioxidant opinion, EFSA has encountered claims relating to *healthy aging*.

²⁸ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) claiming biotransformation of xenobiotic substances (ID 1378, 2388, 2401, 3900, 3942, 4039, 4510, 4513, 4544, 4628, 4639), “elimination”, “cleansing” and “purification” (ID 1347, 4024, 4442, 4457), elimination of heavy metals (ID 1887, 3156), and maintenance of normal bowel function (ID 4039) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1733

²⁹ Scientific Opinion on the substantiation of health claims related to selenium and maintenance of normal hair (ID 281), maintenance of normal nails (ID 281), protection against heavy metals (ID 383), maintenance of normal joints (ID 409), maintenance of normal thyroid function (ID 410, 1292), protection of DNA, proteins and lipids from oxidative damage (ID 1292), and maintenance of the normal function of the immune system (ID 1750) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1727

³⁰ Scientific Opinion on the substantiation of health claims related to selenium and protection of DNA, proteins and lipids from oxidative damage (ID 277, 283, 286, 1289, 1290, 1291, 1293, 1751), function of the immune system (ID 278), thyroid function (ID 279, 282, 286, 1289, 1290, 1291, 1293), function of the heart and blood vessels (ID 280), prostate function (ID 284), cognitive function (ID 285) and spermatogenesis (ID 396) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 on request from the European Commission. EFSA Journal 2009; 7(9):1220

³¹ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and protection of cells from premature ageing (ID 1668, 1917, 2515, 2527, 2530, 2575, 2580, 2591, 2620, 3178, 3179, 3180, 3181, 4329, 4415), antioxidant activity, antioxidant content and antioxidant properties (ID 857,

It is clear from examples of the wording of the claims that such claims refer to the protection against damage from oxidative cellular processes or the maintenance of the body's defences against oxidative damage. A simple request to the submitters could have provided this clarification. Nevertheless EFSA has judged these claims as general and non-specific. Also in this opinion EFSA interprets antioxidant activity, antioxidant content and antioxidant properties as referring to the capacity of foods/food constituents to scavenge free radicals and/or to their reducing capacity, which may be appropriate. However, it then considers that claims made on the antioxidant capacity/content or properties of foods/food constituents based on their capability of scavenging free radicals in vitro refer to a property of the food/food constituent measured in model systems, and that the information provided does not establish that this capability as such exerts a beneficial physiological effect in humans.

We observe that many of the examples of the claims given are considered by EFSA as general and non-specific and therefore not within the scope of the claims to be assessed. As a consequence the evidence provided is not considered.

This is in part the consequence of the way the Article 13 submissions have been compiled in the absence of official guidance. The health relationship was taken as the basis and complemented with examples of how to express this health relationship on the products. It is obvious that the health relationship is general and cannot fit the framework established later on by EFSA. It is also obvious that the examples in many instances are not very specific as they represent mainly language that is to be understood by consumers. It is not appropriate that for the assessment of the claimed effect, EFSA bases itself on these examples and only selects the most specific ones, because they have not been included for that purpose.

It is also not appropriate that EFSA is not able to assess the totality of the evidence to provide an opinion on the role the food or food component has in relation to the health relationship mentioned.

Simply stating that many of these effects are general and non-specific and therefore cannot be assessed is not an acceptable way to deal with this problem. Clarification and guidance on what would be acceptable and offering an opportunity to provide clarification on these submissions would be a more constructive approach given the importance of the effects under consideration (gastro-intestinal, immunological, anti-oxidation, detoxification, etc) that might otherwise lose the possibility to be communicated.

In parallel, the scope and limitations of the EFSA preferred RCT-based approach should be addressed and a more appropriate consideration of the totality of the evidence would seem necessary to consider health effects that do not relate to reducing or increasing disease related markers but to the maintenance of normal physiological functions within the limits of the body's homeostasis. In this respect it would be advisable that the EFSA opinions are considered together with the opinion of experts in the field to establish the exact nature of the health effects. We look very much forward to the guidance that EFSA has announced on claims relating to antioxidants but consider that the guidance and technical meeting on gut

1306, 2515, 2527, 2530, 2575, 2580, 2591, 2629, 2728, 4327, 4365, 4380, 4390, 4394, 4455, 4464, 4507, 4694, 4705), protection of DNA, proteins and lipids from oxidative damage (ID 1196, 1211, 1216, 1306, 1312, 1440, 1441, 1666, 1668, 1692, 1900, 1914, 1948, 2023, 2158, 2517, 2522, 2527, 2575, 2591, 2620, 2637, 2639, 2663, 2860, 3079, 3276, 3564, 3818, 4324, 4329, 4351, 4397, 4416, 4424, 4507, 4527, 4528, 4542, 4611, 4629, 4659) and bioavailability of anthocyanins in black currants (ID 4220) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1752

and immune function was rather disappointing, as the discussions made it clear that the RCT and risk factor based approach adopted is not capable to cover the whole spectrum of beneficial effects in this area. Until this issue is solved we feel it inappropriate to take decisions to include any of these claims in the register of rejected claims.

We would also call on the EC and the Member States to consider this issue of claims characterisation as a risk manager. Indeed, it was their interpretation that led to claims such as ‘*contains antioxidants, probiotics, etc*’ being considered as health claims rather than nutrition claims. It is now the EFSA approach that prevents such claims to be accepted because they are not sufficiently specific. We would consider that such statements could be considered as generic descriptor of a group of ingredients, which could be addressed through the application of Article 1.4 of the NHCR or alternatively by an adaptation of the EC guidance document of 14 December 2007.

Finally, we would like to observe that since the NHRC allows for general, non-specific benefits of nutrients or foods for overall good health or health-related well-being, claims that are rejected because EFSA has considered them non-specific should not be included in the register as rejected claims.

The selective choice of example claims as claims to be assessed sometimes leads to the selection of health effects that are not supported by the evidence whereas the general health relationship is

The fact that EFSA makes decisions to interpret the evidence on the basis of the example wording, can lead to odd situations.

- **Conjugated linoleic acid (CLA)**³²: In its CLA opinion, EFSA addresses a number of health effects taken from the various submitted entries. These include: *maintenance or achievement of a normal body weight, increase in lean body mass, increase in insulin sensitivity, protection of DNA, proteins and lipids from oxidative damage, and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination*. It does not conclude positively on any of these effects.

It is strange however that one health effect, also included in the submissions, “*reduction of body fat*” was not considered although it is, according to the submitter, the main demonstrated effect for CLA. The reasons for EFSA not to consider this specific effect, while many others have been considered are not clear. A consideration of the totality of the evidence would have been able to identify the most pertinent health effect for this substance.

³² Scientific Opinion on the substantiation of health claims related to conjugated linoleic acid (CLA) isomers and contribution to the maintenance or achievement of a normal body weight (ID 686, 726, 1516, 1518, 2892, 3165), increase in lean body mass (ID 498, 731), increase in insulin sensitivity (ID 1517), protection of DNA, proteins and lipids from oxidative damage (ID 564, 1937), and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination (ID 687, 1519) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1794

The choice of claims taken for assessment is biased towards claims indicating improvements of physiological functions rather than maintenance

Also in this 3rd batch of opinions we see examples of the fact that EFSA considers effects relating to an improvement rather than to maintenance of a function.

For essential nutrients, maintenance claims are accepted based on the fact that these substances are essential for a number of specific bodily processes or cellular functions. EFSA even goes beyond the direct effects of these substances as co-factors for the functioning of enzymes that mediate biochemical pathways and considers broader effects on the body, including e.g. tiredness and fatigue and immune function.

However, for health effects relating to other substances, improvements of physiological functions are often expected, effects that a number of substances may not possess.

- **Calcium**²³: In its calcium opinion EFSA accepts the role of calcium in the *normal regulation of cell division and differentiation* based on the evidence available from consensus opinions/reports from authoritative bodies and reviews, although it is clear that calcium is not improving or increasing cell division. Yet such claims are accepted while for non-essential substances the focus of the evidence needs to be on improving or increasing such bodily functions.
- **EPA/DHA**³³: In the EPA/DHA opinion, skin health is translated not to *maintenance of normal skin* (as is the case in the Vitamin E opinion³⁴) but to *protection of the skin from photo-oxidative (UV-induced) damage*.
Also in this opinion, immune function and normal immune system function are translated not into *maintenance of the normal function of the immune system* (as is the case in the Vitamin C opinion²⁴) but to *supporting a normal/healthy immune function in the context of decreasing the level or production of eicosanoids, arachidonic acid-derived mediators and pro-inflammatory cytokines*, which is then not judged to be beneficial.
- **Zeaxanthin**³⁵: In the opinion relating to zeaxanthin and eye health, EFSA (correctly) assumes that the claimed effect refers to *maintenance of normal vision*. A positive opinion on the cause-effect

³³ Scientific Opinion on the substantiation of health claims related to eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), docosapentaenoic acid (DPA) and maintenance of normal cardiac function (ID 504, 506, 516, 527, 538, 703, 1128, 1317, 1324, 1325), maintenance of normal blood glucose concentrations (ID 566), maintenance of normal blood pressure (ID 506, 516, 703, 1317, 1324), maintenance of normal blood HDL-cholesterol concentrations (ID 506), maintenance of normal (fasting) blood concentrations of triglycerides (ID 506, 527, 538, 1317, 1324, 1325), maintenance of normal blood LDL-cholesterol concentrations (ID 527, 538, 1317, 1325, 4689), protection of the skin from photo-oxidative (UV-induced) damage (ID 530), improved absorption of EPA and DHA (ID 522, 523), contribution to the normal function of the immune system by decreasing the levels of eicosanoids, arachidonic acid-derived mediators and pro-inflammatory cytokines (ID 520, 2914), and “immunomodulating agent” (4690) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1796

³⁴ Scientific Opinion on the substantiation of health claims related to vitamin E and protection of DNA, proteins and lipids from oxidative damage (ID 160, 162, 1947), maintenance of the normal function of the immune system (ID 161, 163), maintenance of normal bone (ID 164), maintenance of normal teeth (ID 164), maintenance of normal hair (ID 164), maintenance of normal skin (ID 164), maintenance of normal nails (ID 164), maintenance of normal cardiac function (ID 166), maintenance of normal vision by protection of the lens of the eye (ID 167), contribution to normal cognitive function (ID 182, 183), regeneration of the reduced form of vitamin C (ID 203), maintenance of normal blood circulation (ID 216) and maintenance of normal scalp (ID 2873) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1816

³⁵ Scientific Opinion on the substantiation of health claims related to zeaxanthin and maintenance of normal vision (ID 1684, 2169, 2888) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal

relationship between vitamin A (and beta-carotene as a precursor of vitamin A) and maintenance of normal vision was accepted already as part of the 1st batch of opinions³⁶. However, in assessing the evidence for this effect for zeaxanthin (and other substances such as lutein), EFSA is looking for evidence of an improvement of vision upon supplementation with zeaxanthin. This was also the case for lutein as part of the 2nd batch of opinions³⁷.

The main body of evidence is related to the fact that zeaxanthin is a component of the macular pigment in the eye, an observation confirmed by EFSA in its opinion. This is also confirmed from the example of wording in the entry: *‘An optimal intake of zeaxanthin contributes to eye health/supports normal vision/absorbs blue light and scavenges reactive oxygen species in the eye (lens, retina) and, therefore, helps to maintain a healthy retina/stabilizes membranes and, therefore, contributes to make retinal membranes more resistant against damage by light. (Together with lutein) zeaxanthin is actively accumulated in the healthy macula to the highest concentration of carotenoids found in the human body. A sufficient supply therefore contributes to maintaining the integrity and health of this part of the retina which is most essential for optimal visual performance/(together with lutein) helps to improve visual performance at dim lighting conditions.’*

Furthermore, the epidemiological evidence is considered in the light of an association between zeaxanthin and age-related macular degradation (AMD). It is therefore not surprising that EFSA did not come to the conclusion that a cause-effect relationship is established as it has basically chosen to look for an effect that the existing evidence does not support.

Protein¹² and BCAA³⁸. In the opinion on protein, EFSA concludes that a cause and effect relationship has been established between the dietary intake of protein and the growth or maintenance of muscle mass. However, in the opinion on BCAA (Branched-Chain Amino Acids, which are essential amino acids), EFSA comes to a different conclusion. It concludes that a cause and effect relationship has not been established between the consumption of BCAA and growth or maintenance of muscle mass over and above the well-established role of protein on the claimed effect. Nevertheless, in both cases, EFSA assumed the same health effect (growth or maintenance of muscle mass) and confirmed that this is a beneficial physiological effect. It clearly shows that the focus of the assessment is not on the maintenance of physiological functions but on improvement. Based on the opinion, a cause effect relationship between BCAA and maintenance of physiological functions should have been accepted.

Those examples indicate that the expectations of EFSA relating to the scientific evidence for health effects of other substances are too high. They expect clinical research that is not available at this moment in support of health effects that are too ambitious and that were not

2010;8(10):1724

³⁶ Scientific Opinion on the substantiation of health claims related to vitamin A and cell differentiation (ID 14), function of the immune system (ID 14), maintenance of skin and mucous membranes (ID 15, 17), maintenance of vision (ID 16), maintenance of bone (ID 13, 17), maintenance of teeth (ID 13, 17), maintenance of hair (ID 17), maintenance of nails (ID 17), metabolism of iron (ID 206), and protection of DNA, proteins and lipids from oxidative damage (ID 209) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2009; 7(9):1221

³⁷ Scientific Opinion on the substantiation of health claims related to lutein and maintenance of vision (ID 1603, 1604, 1931) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010; 8(2):1492

³⁸ Scientific Opinion on the substantiation of health claims related to branched-chain amino acids (BCAA) and growth or maintenance of muscle mass (ID 442, 444, 445, 447, 448, 451, 1478), attenuation of the decline in muscle power following exercise at high altitude (ID 443), faster recovery from muscle fatigue after exercise (ID 447, 448, 684, 1478), improvement of cognitive function after exercise (ID 446), reduction in perceived exertion during exercise (ID 450) and “healthy immune system” (ID 449) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1790

intended to be the subject of the submissions to the Article 13.1 list in the first place. There is a clear need to re-address the term of the totality of the evidence and to assess the current state of knowledge and the effects that are plausible based on all evidence available.

This could/should be done in collaboration with the experts in the field and would enable to delimit the boundaries of the health effect. This was the spirit with which the Article 13 list was compiled. We would call upon the EC to consider such an alternative approach as we believe it is in line with the proportionality of the procedures and would enable communication on a broader spectrum of health effect. After all, many of these effects are useful for the consumer to know, even though they have not been tested in the same way as pharmaceuticals.

Certain health effects are considered not to be beneficial based on unclear criteria and the evidence is not considered in these cases

EFSA has identified the vast majority of claimed effects to be either beneficial or potentially beneficial to health. Nevertheless, some effects are not judged to be beneficial. These include effects related to diuretic function (*water elimination from the body*) and to changes in parameters of the immune system (e.g. *stimulating macrophages* and *increasing circulating lymphocytes*) and *antioxidant properties*. Another important example of a health effect considered as non-beneficial is the *increase of potentially beneficial microorganisms in the gastrointestinal tract*. EFSA indicates this is a judgment, but there are no or limited criteria available. In some cases more explanation would be welcome, since if a claim is judged not to be beneficial, the evidence is simply not addressed.

- **Renal water elimination³⁹**: In this opinion, EFSA considers that the evidence provided does not establish that an *increase in renal water elimination* potentially leading to a negative fluid balance is a beneficial physiological effect for the general healthy population. The criteria underlying such this judgment are not clear. We consider that renal water elimination is essential to eliminate waste products from the body and does not necessarily leads to negative fluid balance. We therefore would think that support of the excretory function of the kidneys might be beneficial for health. In the same opinion, EFSA considers that claims referring to *kidney and urinary health* are not sufficiently clear and non-specific. We consider that such claims refer to the support or maintenance of healthy or normal kidney and urinary function and are surprised this is not accepted as beneficial by EFSA. Finally, referring to effects in this opinion related to the *treatment/prevention of renal gravel/kidney stones and urinary tract infections* EFSA indicates that such effects are related to the prevention or treatment of a disease. The context of these two claims however clearly shows that these effects are referred to in the context of the maintenance of kidney function and are not meant as preventive or curative claims. Nevertheless, while the statement “*prevention of urinary tract infection*” would indeed be considered as a preventive claim, health effects showing a decreased incidence of such infections should be acceptable as health claims, in the same way as is discussed in relation to the upper respiratory tract.

³⁹ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) claiming an increase in renal water elimination, “kidneys health”, “urinary health”, “bladder health”, “health of lower urinary tract”, “blood health”, “elimination”, “urinary system benefits” and/or “supports/promotes the excretory function of the kidney”, and treatment/prevention of renal gravel/kidney stones and urinary tract infections pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1742

- **Probiotics⁴⁰**: Again in this batch of opinions, EFSA rejects a number of probiotics that had submitted claims relating to *contains prebiotic/has prebiotic effect, beneficial effect on intestinal microflora, gut integrity, digestion, intestinal bifidobacteria, prebiotic effect, prebiotic and intestinal health*. It is obvious from this, previous opinions and the outcome of the EFSA technical meeting organized on 2 December 2010 in Amsterdam, that EFSA has a narrow interpretation on what would constitute beneficial effects from probiotic bacteria and that this view is not necessarily shared by academic experts in the field. In the context of the proposed wordings, EFSA assumes that the claimed effects refer to aspects related to increasing numbers of beneficial/probiotic bacteria but does not accept this as a beneficial effect. Only a decrease of potentially pathogenic gastro-intestinal microorganisms is considered as a potential beneficial physiological effect.

We feel this interpretation is overly restrictive. The FAO/WHO definition⁴¹ specifies that probiotics are “live microorganisms which when administered in adequate amounts confer a health benefit on the host”. This implies that to be considered as probiotics, the microorganisms must 1. have the capacity of surviving passage through the digestive tract; 2. be capable to proliferate in the gut and 3. exert beneficial effects (which are mostly strain-specific). Health effects considered by this consultation included:

- Efficient action in case of acute diarrhea mainly caused by rotaviruses in children
- Also effects on enteropathogens, traveler’s diarrhoeas and antibiotic associated diarrhoeas (*C. difficile*) are acknowledged.
- In particular, the guidance specifically recognises that the use of probiotics entails administration of exogenous commensal microorganisms (that is probiotics) to restore the microflora to one that more closely reflects the normal flora prior to antibiotic therapy.

We feel that the opinion of EFSA on what to accept as beneficial is hampered by the absence of clear guidelines and would benefit from further clarification. We feel that the consultation process initiated by EFSA, be it a good initiative, is nevertheless not satisfactory because it excludes a genuine scientific discussion with experts in the field. The guidance that still has to be published in its final form based on the outcome of the consultation and discussions of the meeting presents a unilateral view of a few scientists and is not the result of a consensus process that is usually the basis for scientific recommendations. We have noted that academic experts have started openly disagreeing with EFSA’s approach⁴². We believe this is a development that leads to undermining the credibility of EFSA and therefore of the EU approach in this area. It shows the need to consider health effects in a broader context and also to include and value the views of the scientists that actually do the research and are experts in their respective discipline. We would urge the EC to start considering how the opinion of these experts can be brought into the process.

Conclusion:

The strong focus of EFSA on well-defined health effects, mostly relating to improvement of

⁴⁰ Scientific Opinion on the substantiation of health claims related to various food(s)/food constituents(s) and increasing numbers of gastro-intestinal microorganisms (ID 760, 761, 779, 780, 779, 1905), and decreasing potentially pathogenic gastro-intestinal microorganisms (ID 760, 761, 779, 780, 779, 1905) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1809

⁴¹ FAO/WHO. 2001. Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria.

⁴² See www.gut-health.org

physiological functions is not compatible with the scope of the Article 13 list. It often leads to a very narrow interpretation of studies considered as acceptable. Furthermore, in many cases the health effects are judged to be non-specific and the evidence is not considered at all.

Together with the focus of well-defined substances, this approach stems from the choice of EFSA to rely almost exclusively on RCTs to demonstrate statistically and biologically significant changes of intake on markers, mostly considered as risk factors for diseases. This pharmaceutical-style approach was not the anticipated approach for the industry in compiling its submissions.

And we feel this may not be the best approach to validate the benefits of food components for health. As shown by the examples, a number of potentially valuable health effects are ignored or do not make a chance under this approach. We would therefore call upon the EC to reflect if this was the goal of the claims legislation and initiate discussions, in particular involving the science community to correct the inconsistencies and limitations we observe. There are alternative approaches being applied by others that enable a broader spectrum of health effects of foods, categories of foods, groups of food components and even diets to be recognized by a consideration of the totality of the data and weighing this data to indicate the strength, consistency and plausibility of the effect, in analogy to the way that public health recommendations are being considered.

3. Nature of the evidence

Our guidance⁴ indicated that evidence to support a health claim should be based on studies in humans and that animal and in vitro studies are useful as supporting evidence but are not sufficient on their own to substantiate a claim. Among studies in humans, the randomized, placebo-controlled, double-blind intervention study provides the strongest evidence.

However, the document also acknowledged that it is not always possible to conduct such intervention studies on foods and food components. It specifies that epidemiological and observational data are generally accorded a lower weighting of evidence. However, in some cases epidemiological and observational data are the only type of evidence available to support health claims, and indeed these studies often form the main source of data on which dietary guidelines are based. Epidemiological and observational studies can provide sufficient evidence if the data are consistent, statistically significant and biologically plausible, especially if supported by appropriate animal and in vitro studies.

Furthermore, much value was given to authoritative bodies, recognized textbook, meta-analysis, monograph, critical and systematic Cochrane reviews, next to individual studies.

We considered that only on specific cases the food or food component and the health relationship must be supported by individual scientific papers, and these papers will need to be subject to a more detailed review, as suggested in Section 3.5 of the guidance document.

Furthermore, in the section on references, our guidance stated that if the health claims are not underwritten by authoritative statements, recognized textbooks and monographs, then individual papers including reviews, meta-analyses and individual study reports should be referenced. We observe that EFSA ignores largely authoritative sources for non-essential substances and foods if no scientific data are included and only assesses claims on the basis of individual RCTs.

Our approach to the assessment of claims contained in the Article 13.1 list therefore foresaw that the conclusions should illustrate the weight of, and the strength and consistency of the evidence so that it can be consistent with the use of the term ‘generally accepted scientific evidence’. It supported the approach to present and grade the scientific evidence in support of health claims used by the US Food and Drugs Administration⁴³ and in evidence-based approaches to establishing dietary guidelines and nutrition-related public health issues (World Cancer Research Fund⁴⁴; World Health Organization⁴⁵; King⁴⁶). A similar system was at the time being developed by the competent authorities of The Netherlands⁴⁷.

To quote the guidance document:

“As noted above, evidence from epidemiological human trials and observational studies in humans has often been the primary source of information for dietary guidelines and for some health claims since, under ‘real world’ conditions, conducting RCTs is very challenging and often impossible because of enormous logistical, ethical and cost challenges.

Hence, as the process of scientific discovery evolves, the assessment of the evidence base must reflect real world research and not depend solely on ‘ideal world’ research or efficacy-based RCTs.

It is to be hoped that the EFSA will find a pragmatic solution to the assessment of the scientific evidence and will be able to reflect the degree of scientific certainty of the health relationship by using a grading of evidence methodology for the evaluation of health claims. The substantiating evidence should be proportionate to the claim and reflect emerging, as well as consensus science.”

The analysis of examples of EFSA opinions discussed in this paper, clearly illustrates that EFSA has not found this pragmatic solution and that the approach therefore needs readjusting. We would call on the EC to initiate such reflections and involve academic experts in the field in this work. The model we have developed can also be of help²².

4. Limitations of the Regulation and its interpretation

We would finally also shortly want to comment on an aspect that has become painfully clear during the EFSA technical meeting of 2 December. This concerns the restrictions imposed by the legislation, or rather by its current interpretation relating to the obligation to address risk

⁴³ US Food and Drug Administration 2003. Consumer health information for better nutrition initiative. Task Force Final Report. Attachment B—Interim evidence-based ranking system for scientific data guidance: interim evidence-based ranking system for scientific data; Attachment E—Interim procedures for qualified health claims guidance: interim procedures for qualified health claims in the labelling of conventional human food and human dietary supplements.

<http://www.fda.gov/Food/LabelingNutrition/LabelClaims/QualifiedHealthClaims/QualifiedHealthClaimsPetition/s/ucm096010.htm>

⁴⁴ World Cancer Research Fund/American Institute for Cancer Research. 1997. Food, nutrition and the prevention of cancer: a global perspective. Washington DC, USA

⁴⁵ World Health Organization (WHO). 2002. Diet, nutrition and the prevention of chronic diseases: report of a joint FAO/WHO expert consultation. WHO Technical Report Series 916, Geneva, Switzerland

⁴⁶ King, J.C. 2007. An evidence-based approach for establishing dietary guidelines. *Journal of Nutrition* 137: 480-483

⁴⁷ Netherlands Proposal for a systematic approach for a generic list of Health Claims. Draft December 2004.

factors for the substantiation of claims.

We believe there are two important comments to be made:

- The EC in its guidance note of 14 December 2007⁷ have agreed on an interpretation of reduction of disease risk claims (RDRC). RDRC are claims that refer to a reduction of a risk factor, irrespective of whether such claims mention the specific disease. We believe this interpretation is not correct for several reasons:
 - The definition of RDRC specifically makes reference to a disease: “reduction of disease risk claim’ means any health claim that states, suggests or implies that the consumption of a food category, a food or one of its constituents significantly reduces a risk factor in the development of a human disease”.
 - RDRC are claims that had not been allowed until the Claims Regulation, which is also the reason why no transition period is foreseen. Nevertheless, certain claims that are now considered as RDRC, including lowering blood cholesterol had been lawfully used on products marketed in several Member States.
 - Article 14 of the MHCR requires the labelling or, if no such labelling exists, the presentation or advertising to bear a statement indicating that the disease to which the claim is referring has multiple risk factors and that altering one of these risk factors may or may not have a beneficial effect. This requirement does not make sense if no name of disease is mentioned in the claim.
 - Linking RDRC to diseases would bring the EU legislation in line with Codex Guidelines⁴⁸ and would be similar as the US approach. That this was the original intention can be seen from a Q&A issued by the EC to accompany its proposal⁴⁹.

We would ask the EC to reconsider its interpretation in this respect and to only consider under Article 14 claims that relate to the reduction of risk factors in association of the corresponding disease.

- The second comment concerns the focus that EFSA puts on the presence of risk factors. This may be in line with a strict interpretation of the regulation, but not necessarily with its intention. At the Technical meeting on Gut and Immune Health, EFSA clarified that if no risk factor is covered by the evidence underlying a claim, the claim cannot be approved, not even if a significant reduction is shown on the actual disease⁵⁰. This is clear from the example that when a probiotic micro-organism would show a decrease in the incidence of infection or symptoms associated with infection, but no concomitant reduction of the corresponding pathogenic micro-organism is demonstrated, such claims cannot be assessed under the terms of the NHCR.

We believe that what matters is the reduction of disease risk, irrespective of whether a reduction of a disease risk factor is demonstrated or not and would urge the EC and the Member States to interpret the law in this light. And should this not be possible, to take steps

⁴⁸ Codex Alimentarius. 2004. Guidelines for use of nutrition and health claims. CAC/GL 23-1997, Rev. 1-2004

⁴⁹ European Commission. 2003. MEM0/03/188: The proposed Regulation on health & nutrition claims: Myths & Misunderstandings. http://ec.europa.eu/food/food/labellingnutrition/resources/press315_en.pdf

⁵⁰ EFSA. 2010. Draft guidance on the scientific requirements for health claims related to gut and immune function. Lines 203-205. <http://www.efsa.europa.eu/en/consultationsclosed/call/nda100928.pdf>

to amend the law to make such claims fall under it. If not, some health effects with a considerable benefit for public health may not be allowed to be communicated and much research in the field of probiotics and potentially other fields will not be able to be used.

General Conclusions

The analysis of the 3rd batch of EFSA opinions have made clear that at least half of the claims of the industry list have been rejected because they do not meet the format established by EFSA after the submissions had been made. These requirements were not known and now result in a rejection of claims submission for formalistic reasons without assessment of the scientific data. The examples taken from the EFSA opinions clearly show that many negative opinions stem from this fundamental discrepancy.

Furthermore, the examples also show that the approach adopted by EFSA has considerable limitations to assess certain types of health benefits. We do not dispute that the RCT-based approach represents the highest scientific standard possible to demonstrate cause-effect relationships. However, for such trials to be possible, it is necessary that the intervention is well characterised, and the study can be carefully controlled for factors that can bias the results. It is also necessary that relevant biological parameters are available and that differences are measurable and both statistically and biologically relevant. This approach is appropriate to assess the efficacy for pharmaceutical substances, but perhaps less adapted to nutrition, where it is only capable of assessing effects of interventions/supplemental intake of well-defined compounds on measurable biological or physiological parameters (which are in most cases biomarkers related to abnormal situations and diseases).

We therefore think it essential that more reflection is given to these problems, that those claims are not included as rejected in the register to come, and that clarity is provided and claims can be resubmitted or complemented with additional information and clarification via the Article 13.4 process. This procedure is already envisaged for insufficiently characterised probiotics and insufficient claims. It would be appropriate to enable this also for other claims, based on the EFSA opinions. For Article 13.1 claims there is no official opportunity to comment on opinions. Nevertheless, to safeguard the rights of submitters, it would be appropriate that the EC enables comments to be sent and be considered. If not, we feel that a large number of submissions have not been correctly and reasonably treated under the Article 13.1 process, which is not justified.

This pharmaceutical-style approach was not anticipated when the industry federations joined forces to coordinate submissions from their members, based on guidance that assumed the possibility that claims for individual foods, categories of foods, groups of food components and even diets that share the same characteristics would be able to be assessed by considering the totality of the data and weighing these data to indicate the strength, consistency and plausibility of the effect, in analogy to the way that public health recommendations are being considered. We strongly believe that a system that is not able to accept a claim for dietary fibre as such has a fundamental weakness and efforts should be undertaken to try and correct this abnormality.

The outcome of a number of EFSA opinions, discussed in this paper, clearly demonstrates the limitations of the RCT-based approach:

- EFSA considers characterisation in an absolute way and only considers studies performed with individual substances or foods with well-defined amounts of those substances as pertinent. This makes generally accepted claims for e.g. dietary fibre, no longer possible. It leads to a situation where:
 - The process is not able to reach positive conclusions on complex foods or mixtures of food components in the diet (e.g. dietary fibre, whole grain)
 - The strong focus on well-defined substance characterisation leads EFSA to consider much of the observational studies that have been performed with the foods as such as not pertinent for the assessment of the claims (e.g. protein, soy protein, tea).
 - The strong focus on pure food components makes it difficult to accept natural variability associated with the composition of foodstuffs (e.g. pomegranate, propolis).
 - The strong focus on well characterised food components favours effects that can be demonstrated by interventions with substances on top of the normal diet but largely fails to assess beneficial effects of modifications of the diet itself (e.g. Hydroxypropylmethylcellulose and pectin as compared to glycaemic index and protein).
- The main subject of an Article 13 submission was the health relationship. This was accompanied by examples of possible wording. We observe that EFSA has largely ignored the health relationship (often considered insufficiently specific) and focused on specific wordings to assess. This has led to a situation where:
 - Lack of acceptance of the health relationship as sufficiently characterised to be assessed is eliminating whole areas of health benefits from the scope of the NHCR (e.g. immune function, digestive function, energy and vitality, biotransformation of xenobiotic substances, antioxidants).
 - The selective choice of example claims as claims to be assessed sometimes leads to the selection of health effects that are not supported by the evidence whereas the general health relationship is (e.g. Conjugated linoleic acid).
 - The choice of claims taken for assessment is biased towards claims indicating improvements of physiological functions (effects the substances may not possess) rather than maintenance (e.g. EPA/DHA, Zeaxanthin).
 - Certain health effects are considered not to be beneficial based on unclear criteria and the evidence is not considered in these cases (e.g. Renal water elimination, probiotics).

It is obvious that these elements considerably limit the potential of a number of health effects to be validated. We observe that a number of claims have been favourably assessed by EFSA despite this reliance of RCTs. We note however that these claims are based on parameters relating to reduction of disease risk or are either factual information (cfr. lactase) or generally accepted knowledge on the functions of vitamins and minerals and other essential nutrients. What we lack until now is positive opinions for health effects relating to food components' roles in the maintenance of a body function (in the absence of disease related parameters).

We therefore think it essential that more reflection is given to these problems. We do not consider that a revision of the approach would automatically result in many of the assessed claims to be accepted, as obviously the evidence submitted for many claims is weak. Nevertheless, we strongly believe that a number of assumptions made by EFSA unduly limit the potential of a number of specific health benefits to be accepted. The exclusive reliance on RCTs on well characterised constituents of foods to demonstrate statistically and biologically significant changes of supplemental intake on markers, mostly considered as risk factors for diseases, may not be the best approach to validate the benefits of many food components for the maintenance of a healthy life.

We therefore think it is not appropriate to continue before a fundamental reassessment has taken place. Such a reassessment must at least consider the following elements, which we would therefore ask the EC and the Member States to consider:

- Not to take decisions to prohibit claims on the basis of these EFSA opinions but allow that these claims are resubmitted for evaluation in the same way as this is intended to be allowed for insufficiently characterised probiotics and insufficient claims.
- For such resubmission, accept that the procedure of Article 13.4 is appropriate and not to adopt a systematic obligation to submit a dossier under the Article 13.5 procedure.
- To address the problems with the scientific approach raised in this paper and enable discussions with EFSA to apply alternative approaches to consider the totality of the evidence and weigh the evidence to provide a balanced view on the strength, consistency and plausibility of the health benefit of food components that are used by other organisations and have also been explained in the claims model we developed²².
- To involve in these discussions and on specific topics the views of academic experts in the field to achieve a consensus based acceptance of the health effects under consideration.
- To consider that claims that received a negative opinion because of the lack of characterization of the substance cannot be considered as claims that can be included in the register of rejected claims. Likewise, that claims that are rejected because the health effects are considered general and non-specific should not be included in the register given that the NHCR explicitly allows such claims to be made if accompanied by an approved claim.

- To resolve the current vagueness and lack of clarity on the interpretation of what is accepted as a sufficiently characterised food or food component or a sufficiently specific health effect and what is not.
- To consider claims such as ‘*contains antioxidants, probiotics, etc*’ being considered as health claims but having no chance of being accepted under the EFSA assessment as well understood generic descriptors of groups of ingredients, which could be addressed through the application of Article 1.4 of the NHCR or alternatively by an adaptation of the EC guidance document of 14 December 2007.

We would offer our constructive help to make this happen and refer back to the model²² that we developed in 2009, which may give useful input into the various elements to consider.

We plead for a broader consideration of the totality of the evidence as opposed to the selective approach adopted by EFSA.