Botanical Health Claims on Foods and Food Supplements in the EU

EHPM proposal

Abstract

The EU Nutrition and Health Claims Regulation prohibits health claims on foods, including Food Supplements, unless authorised by reference to either generally accepted science or a high quality scientific assessment of independently provided data. The methodologies developed and applied by EFSA in pursuance of these objectives have been effective in authorising claims for nutrients based on generally recognised science (*e.g.* vitamins and minerals), but not so effective for the many other claims associated with more complex foodstuffs (*e.g.* those obtained from plants and other vegetative organisms – 'botanicals'). Assessment of botanical health claims has therefore been put on hold. This paper describes how the current assessment process applied by EFSA can be adapted to the over 2000 botanical health claims that are on-hold by using a graded approach, which reflects the evidence for the claim in the wording. Three grades of health claim are proposed: 'scientifically established' claims based on conclusive clinical evidence; 'well-supported claims' that reflect significant developments in modern science and experience; 'traditional use claims', similar to those already in use for Traditional Herbal Medicinal Products (THMP), which are based on recognised and scientifically plausible traditions of use. The different types of evidence required to substantiate claims are identified and the level of this evidence required for each type of claim is specified: botanical substances must be appropriately characterised; stringent scientific evaluation must be applied; and the honesty, accuracy and meaningfulness of claims must be assured. This approach has a number of important benefits: it resolves the legal anomaly with the treatment of THMPs while benefiting from the legal robustness of the THMP approach; it provides an incentive to the small to medium sized businesses (SMEs) that predominate in the food sector, and especially in the food supplement sector; it encourages all businesses to engage in research and development by providing a practical solution from which they can benefit; and it provides consumers with controlled information that they are looking for on the food, and in particular the food supplements, that they purchase and consume.

Contents

p2 Abstract
p4 1. INTRODUCTION

p5 2. BACKGROUND
p5 2.1 The Nutrition & Health Claims Regulation (EC/1924 2006) (NHCR).
p5 2.2 Industry Concerns with the NHCR
p5 2.3 Review of Progress 12 years after the Enactment of the NHCR
p6 2.4 A Graded Approach to Botanical Health Claims
p7 2.5 The Relevance of Botanical Health Claims to Food Supplements.

p8 3. KEY ISSUES FOR BOTANICAL HEALTH CLAIMS
p8 3.1 Legal and Regulatory Context of the Present Proposals
p8 3.2 Definition of Botanical
p9 3.3 The Need to Re-Prioritise Informed Consumer Choice.
p9 3.4 The Understanding of Botanicals and their Effects on Human Health
p10 3.5 The Graded Approach to Botanical Health Claims
p11 3.6 The Levels of Evidence applied to Graded Health Claims
p12 3.6.1 Application of the Levels of Evidence to the three Grades of Botanical Health Claims

p13 4. THE EVALUATION OF BOTANICAL HEALTH CLAIMS
p13 4.2 Characterisation of the Botanical
p13 4.2.1. General Principle
p14 4.3. Evaluation of the Wording of Botanical Health Claims
p14 4.3.1 General Principles Applied
p14 4.3.2 Conformance with the Principles of the NHCR
p14 4.3.3 Scientific Assessability of Functional Claims (EFSA Guidelines 7.2.1)
p15 4.3.4 The Wording of Scientifically Established Health Claims (Grade A)
p15 4.3.5 The Wording of Well-Supported Health Claims (Grade B)
p15 4.3.6 The Wording of Traditional Use Health Claims (Grade C)
p16 4.4.1 The Evaluation of Grade A Claims on the basis of generally accepted Science
p16 4.4.2 The Evaluation of Grade B Claims on the basis of Well-Supported Science
p17 4.4.3 Evaluation of Grade C Claims on the basis of Traditional Use and Scientific Plausibility

p18 5. CONCLUSIONS

p20 Appendix I Data Collection Module

1. INTRODUCTION

As presently implemented, the Nutrition and Health Claims Regulation (NHCR) is meeting the needs of neither consumers nor the industry – nor, arguably of regulators:

- Consumers are not being provided with the information they are looking for on the foods that they purchase and consume;
- The industry is not able to communicate honestly, accurately and meaningfully with consumers about the benefits associated with the foods they produce and supply;
- Regulators are not able to uniformly control the market in a satisfactory way.

The reason for this problem is that the approach to the authorisation of health claims, initially adopted under the NHCR, is excessively restrictive and not practical. Criteria have been adopted that are appropriate for scientifically establishing the role of isolated food constituents in human physiology, but not for explaining the more complex relationships between foods and health. This deficiency is particularly significant for health claims associated with plants or other vegetative organisms, such as algae and fungi, because these 'botanicals' contain not only a broad spectrum of the nutrients required for life and growth, but also a wide range of other biologically active constituents that function to support the normal physiological processes of the body.

This paper reviews these challenges and suggests that the current scientific methodology applied by EFSA to claims evaluation can be adapted to a graded approach capable of assessing and authorising both traditional health claims that are scientifically plausible and more modern health claims that are increasingly scientifically well-supported. In this way a solution can be provided that meets the needs and aspirations of consumers, the industry and regulators alike.

2. BACKGROUND

2.1 The Nutrition & Health Claims Regulation (EC/1924 2006) (NHCR).

In its Preamble, the NHCR aspires to facilitate *informed choice*, alongside *the protection of consumers* and the encouragement of legitimate business in the food industry[2]. However, the actual objectives stated in the Articles of the Legislation only refer to ensuring *the effective functioning of the internal market* and *providing a high level of consumer protection*[3].

In effect the Regulation prohibits health claims on foods, unless authorised following *a scientific assessment of the highest possible standard*[3] and by reference to *generally accepted scientific evidence*[4], and it establishes the general principles to be applied to the use of health claims.

The all-important details of the authorisation process are not given in the NHCR. They were established later by the implementing regulations (EC/353/2008) and by EFSA guidelines, including its *General Scientific Guidance for Stakeholders on Health Claim Applications*[5].

2.2 Industry Concerns with the NHCR

The food industry as a whole had significant reservations about the NHCR from the outset. While recognising the need to address the rapid increase in understanding of the nature of food and its effects on human health, the industry considered that the approach proposed by the NHCR was in danger of being disproportionate and excessively restrictive. The European Health Product Manufacturers Association (EHPM) and its member organizations were particularly concerned that the Regulation was overly influenced by the aspirations and needs of regulators and scientists, and that this would result in an excessively demanding authorization process that did not take adequate account of the needs and aspirations of consumers and industry. In the run-up to the enactment of the Regulation, EHPM therefore promoted a graded approach to health claims and claims evaluation that reflected existing industry and consumer practice, as well as the challenges faced by science when dealing with the complex relationships between food and human health[6].

2.3 Review of Progress 12 years after the Enactment of the NHCR

EHPM's concerns were not reflected in the implementation of the Regulation: only claims that can be established by scientific consensus of proof can be authorized – either by reference to generally accepted science (*e.g.* '*calcium is needed for the maintenance of normal bones*'), or through a body of converging scientific evidence that is confirmed by human studies of sufficient quality and scale to establish scientific consensus of proof (*e.g.* 2 randomised clinical trials at least).

2.3.1 The progress with this approach is reflected in the EU Register of Nutrition and Health Claims[7]. Table 1 (below) is an analysis of the 2524 entries on this register in May of 2018 – 12 years after the enactment of the Regulation.

[2] EC 1924/2006: Preamble 1, 9, 32 & 33
[3] Ibid Article 1.1
[4] Ibid Preambles 23, 11; Articles 5, 6, 13.1, 13.4
[5] Available on the Nutrition and Health Claims page of the EFSA website
[6] *e.g.* The Scientific Substantiation of Health Claims (IADSA 2005)
[7] https://ec.europa.eu/food/safety/labelling_nutrition/claims_en

Table 1: Authorised Claims on EU Nutrition & Health Claims Register – March 2018

Type of Ingredient	Article 13.1 accepted science	Article 13.5 new science	Article 14 child development, disease risk reduction	Totals
Nutrients*	169	1	16	182
Other Substance (including botanicals)	43	1	6	47
Food	3			3
Food Category (*e.g.* Protein, Sugar Replacers)	20	3	4	28
Total**	235	5	26	266

* Nutrients are taken to refer to Vitamins, Minerals, individual Proteins and individual Fatty Acids;

** Second opinions of EFSA on the same health claim are not counted.

Analysis of Table 1:

Only 266 of the 2524 entries on the Register (about 10%) have been authorised.
88% of these authorised claims are based on generally recognised science (Article 13.1);

- Of these, 70% relate to the recognised action of isolated nutrients;
- Less than 1% of authorised claims relate to new claims substantiated under article 13.5 by independently generated scientific evidence;
- Only 3 authorised claims relate to staple foods (yoghurt, walnuts and prunes).

In addition, the vast majority of 'botanical health claims', over 2000, were placed on hold by the Commission in 2010, after it became clear that they were not capable of being assessed/authorised under the existing system.

2.3.2 These outcomes substantiate initial industry concerns about excessively restrictive regulation:

- Industry is not engaging meaningfully with the Regulation;
- Consumers are not being provided with the information they are accustomed to receive and still look for the health benefits of the foods that they purchase;
- Because they are not being provided with this information at point-of-sale, consumers are increasingly seeking it out from uncontrolled sources, like the Internet – undermining legitimate business, destabilizing the internal market and increasing, rather than reducing the risk of being misled.

2.4 A Graded Approach to Botanical Health Claims

In 2012, the European Commission asked Member States to reflect on whether it would be appropriate, as an alternative to the existing approach, to address the large number of botanical health claims, which are currently 'on-hold', by adopting a traditional use approach similar to that in existence under Medicine Law for Traditional Herbal Medicinal Products under Directive 2004/24/EC. EHPM supports this suggestion in principle because:

a. It allows botanical health claims to be consistently addressed in the context of the strong cultures of use that exist in every Member State of the European Union;
b. It allows for a graded approach to the evaluation of scientific evidence that more appropriate-

ly reflects the nature of scientific inquiry into the effects of foods on health.

However, EHPM also recognises that an approach to health claims on foods based on historic traditions alone would not be appropriate because:

i. There is now a requirement under EU Food Law for a high quality scientific assessment of health claims.
ii. The food market is not static – it is continuously evolving to reflect consumer expectation, science and experience; this evolution is more significant than ever for both industry and consumer in the 21st century because of the extraordinary growth in scientific research into food and its effects on health and because both consumers and industry have access to similar information through essentially the same information technology.

EHPM therefore considers that a more graded approach to botanical health claims is needed at this time – an approach that allows for established uses to be reviewed in the context of emerging and consensus science. Three grades of claim are proposed, each supported by appropriate levels of evidence:

A. Scientifically established claims, based on a modified form of the conclusive scientific evidence currently applied by EFSA; the form of such claims is, for example. 'a … contributes to… b'), which the consumer is taken to understand as meaning that consumption of botanical 'a' will produce health benefit 'b';
B. Scientifically well-supported claims, based on a significant body of evidence; the form of such claims is, for instance, 'a can contribute to b', which the consumer understands as meaning that the consumption of botanical 'a' may well produce health benefit 'b', but will not necessarily do so.
C. 'Traditional Use Claims', based on a demonstrated tradition and plausible science; in the form 'a is traditionally used for b', which the consumer is taken to understand as meaning that there is a significant tradition of use, but which in the EHPM proposal also indicates that the traditional use is scientifically plausible.

2.5 The Relevance of Botanical Health Claims to Food Supplements.

EHPM has worked with national representative organisations within the food supplement sector, and with scientific experts, to develop the approach presented herein for the evaluation of health claims for botanicals used in food supplements.

The Food Supplement industry is uniquely positioned to put forward proposals for such botanical health claims because:

i. While other classes of food are also consumed for satiety or pleasure, all food supplements are produced, supplied and used exclusively for their nutritional and physiological effects – which effects typically focus on the promotion of health.
ii. Materials obtained from plants or other vegetative organisms ('botanicals') are particularly important to the food supplement sector because of their versatility and popularity in food supplement form:
    a. Botanicals contain both the nutritional substances required for energy, growth and health, and other biologically active substances that support the normal physiological

processes of the body;

b. Botanicals have strong traditions of use throughout Europe, and are the subject of intensive scientific research and of intense consumers interest.

iii. The standards that the food supplement industry has developed for presenting food products in unit dose form are specifically relevant to claims substantiation (*e.g.* ensuring finished products contain defined levels of specific active ingredients).

3. KEY ISSUES FOR BOTANICAL HEALTH CLAIMS

3.1 Legal and Regulatory Context of the Present Proposals

The broad **legislative context** of the current discussion paper is the making of health claims for botanical foods/food supplements in the European Union. The provisions of EU Food Law therefore apply, including the provisions of the NHCR – including the definitions in the NHCR, the requirement for scientific assessment, the requirement that claims be honest, accurate and meaningful and not meant to mislead.

The **regulatory context** is the general approach to health claims evaluation developed by EFSA, with which the proposals attempt to be broadly consistent.

3.2 Definition of Botanical

Botanical (noun): *'material, preparations or substances obtained from plants or other vegetative organisms, such as algae, fungi or lichen'*[8].

Botanical (adjective): This meaning of the word 'botanical' is also used as an adjective in the present document in association with, for instance, types of food/foodstuff or food supplements, material, preparations or substances.

Botanicals are essentially complex matrices of substances bonded together at a molecular level by the action of living organisms. The chemical profile varies according to species and within species, according to agricultural and climatic conditions, and according to the part used and the form of preparation. Historically the forms of preparation were largely mechanical (*e.g.* cutting, drying, pulverizing, pressing, heating) or by means of simple chemical extraction processes, typically with alcohol and/or water. More sophisticated forms of the same basic processes are increasingly used in more modern times (*e.g.* freeze extraction or the use of other chemical solvents) to produce purified and concentrated forms of a botanical, or to produce botanicals of a more consistent quality whose effects on health can be more accurately studied and measured, and which can be effectively used by the food supplement industry[9], taking due account of the Novel Food Regulation (EU 2015/2283).

[8] Adapted from the definition used by EFSA in EFSA Journal 2009, 7(9):124, when considering the safety of botanicals;
[9] More detailed information on the characterisation of botanicals is given in section 4.2 and also in Chapter 6 of the EHPM Quality Guide, available on the EHPM.org website.

3.3 The Need to Re-Prioritise Informed Consumer Choice.

Article 1 of EU/1169/2011, on the provision of food information to consumers, asserts the fundamental right of consumers to information on the food that they purchase and eat.

> (The regulation) *provides the basis for the assurance of a high level of consumer protection in relation to food information, taking into account the differences in the perception of consumers and their information needs whilst ensuring the smooth functioning of the internal market (Article 1.1).*
>
> *(It) establishes the general principles, requirements and responsibilities governing food information, and in particular food labeling. It lays down the means to guarantee the right of consumers to information and procedures for the provision of food information, taking into account the need to provide sufficient flexibility to respond to future developments and new information requirements (Article 1.2).*

Furthermore, the NHCR itself **aspires** to facilitate informed choice, alongside the protection of consumers and the encouragement of legitimate business in the food industry:

> *"In order to ensure a high level of protection for consumers and to facilitate their choice, products put on the market, including imported products, should be safe and adequately labeled (Preamble 1).*
>
> *"Therefore general principles applicable to all claims made on foods should be established in order to ensure a high level of consumer protection, give the consumer the necessary information to make choices in full knowledge of the facts, as well as creating equal conditions of competition for the food industry "(Preamble 9).*
>
> The Regulation seeks to *stimulate research and development within the agri-food industry in a way that facilitates access to claims by small and medium-sized enterprises (SMEs), taking into account that SMEs represent an important added value to the European food industry in terms of quality and preservation of different dietary habits (Preamble 32 and 33).*

However, the actual **objectives** of the NHCR as stated in Article 1.1 are restricted to just two principles – ensuring the *effective functioning of the internal market, and providing a high level of consumer protection*.

It is the view of the EHPM that limiting the objectives in this way has resulted in excessively **restrictive and impractical regulation**, which not only fails to deliver on its broader aspirations, but actually inhibits legitimate business and the provision of authentic information to consumers – as demonstrated in the analysis of the EU Register of Nutrition and Health Claims at paragraph 2.3.1 above.

3.4 The Understanding of Botanicals and their Effects on Human Health

Botanicals consist of complex matrices of substances with complex effects on health, which vary according to the chemical structure of the starting material, the method of preparation, intake levels and the health status of the consumer. This is the context within which consumers experience health benefits and the context within which they seek information.

Studying single actions of isolated constituents, as required under the present authorization process, provides important insights into the physiological effects of botanicals. However, this is not the only way to ascertain health benefits and, indeed, the study of the effects of isolated constituents is better suited to the study of medical benefits than health benefits:

- Complex botanicals have many physiological effects; the health benefits experienced are not therefore limited to the action of one clinically studied constituent;
- There is wealth of information available on the health benefit of botanicals – some of it scientific; however, only a limited amount of this information is relevant to the study of a specific cause/effect relationship of any one isolated constituent;
- Matrix effects are not the same as the effects of isolated, concentrated constituents;
- The medical methodology used to study the isolated action of substances in experimentally controlled situations is not suited to studying physiological benefits:
    - The medical methodology is designed to study physiological changes of a high amplitude that develop relatively quickly and are relatively simple to identify and measure in a controlled environment, particularly where the measurement relates to dysfunctional changes;
    - However, the amplitude of physiological improvements expected from complex botanical foodstuffs is quantitatively low, requiring the study of larger numbers over longer periods of time with a variety of different methodologies[10] that produce a different quality of evidence.

It is not therefore reasonable, when drafting legislation on the health benefits of foods, to restrict communication just to what has been clinically studied in sufficient detail and isolation to establish scientific consensus of proof of a physiological effect.

3.5 The Graded Approach to Botanical Health Claims

A huge amount of work, worldwide, has been conducted in the field of linking grades of evidence to the strength of a claim. In this area the « GRADE system » (Grade Working Group, 2004)[11] has a predominant position, but is far from being universally recognized as a standard, and many countries or scientific societies prefer to use their own grading system. However, all these grading systems are globally similar and rate the strength of the recommendations or claims on the strength of the evidence according a kind of pyramid where the Randomised Clinical Trial (RCT) has the predominant position. The system reviewed herein is based on the GRADE approach, adapted to taking account the nature of botanicals, their use and the type of evidence that is available for the 3 grades of claim proposed (Diagram 1).

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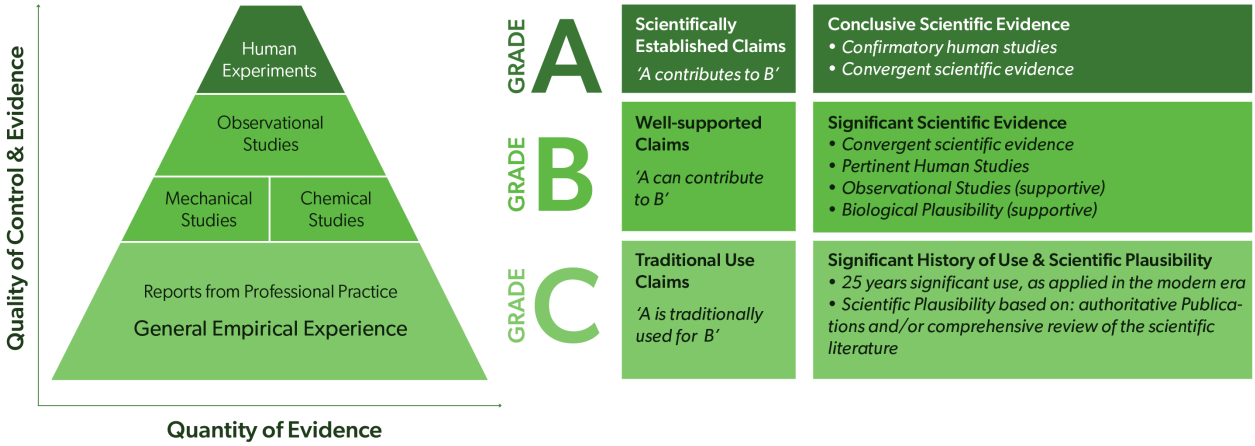
[10] Examples of alternative research methodologies (Allaert):
- Objective analysis of composite criteria linked to well-being
- Studying the relationship between biological criteria and health status
- Quality of life assessment techniques
- Studying the results of well-controlled professional practice

[11] http://www.gradeworkinggroup.org/

Diagram 1: Overview of the Graded Evaluation of Botanical Health Claims



Note on Monographs and Meta-Analyses
These are comprehensive reviews of data, which when officially recognised, remove the need to independently gather and evaluate evidence

3.6 The Levels of Evidence applied to Graded Health Claims

To facilitate consistent evaluation, each grade of claim needs to be assessed by reference to specific, graded levels of evidence – e.g the GRADE system shown in Table 2a.

Table 2a: Grading of evidences according to GRADE Group 2004

Level	Type of Evidence
1a	Evidence from a meta-analysis of randomised controlled trials
1b	Evidence from at least one randomised controlled trial
2a	Evidence from at least one controlled study without randomisation
2b	Evidence from at least one other type of quasi-experimental study
3	Evidence from observational studies
4	Evidence from expert committee reports or experts

In addition to this grading of human evidence, certain types of other evidence needs to be taken into account when dealing with botanicals:

Table 2a: Grading of evidences according to GRADE Group 2004

Sicnificance	Type of Evidence
Supportive	Biological or Mechanistic studies
Prerequisite	Chemical Profiling (for identity and substances of interest)
Supportive	History of use data

3.6.1 Application of the Levels of Evidence to the three Grades of Botanical Health Claims

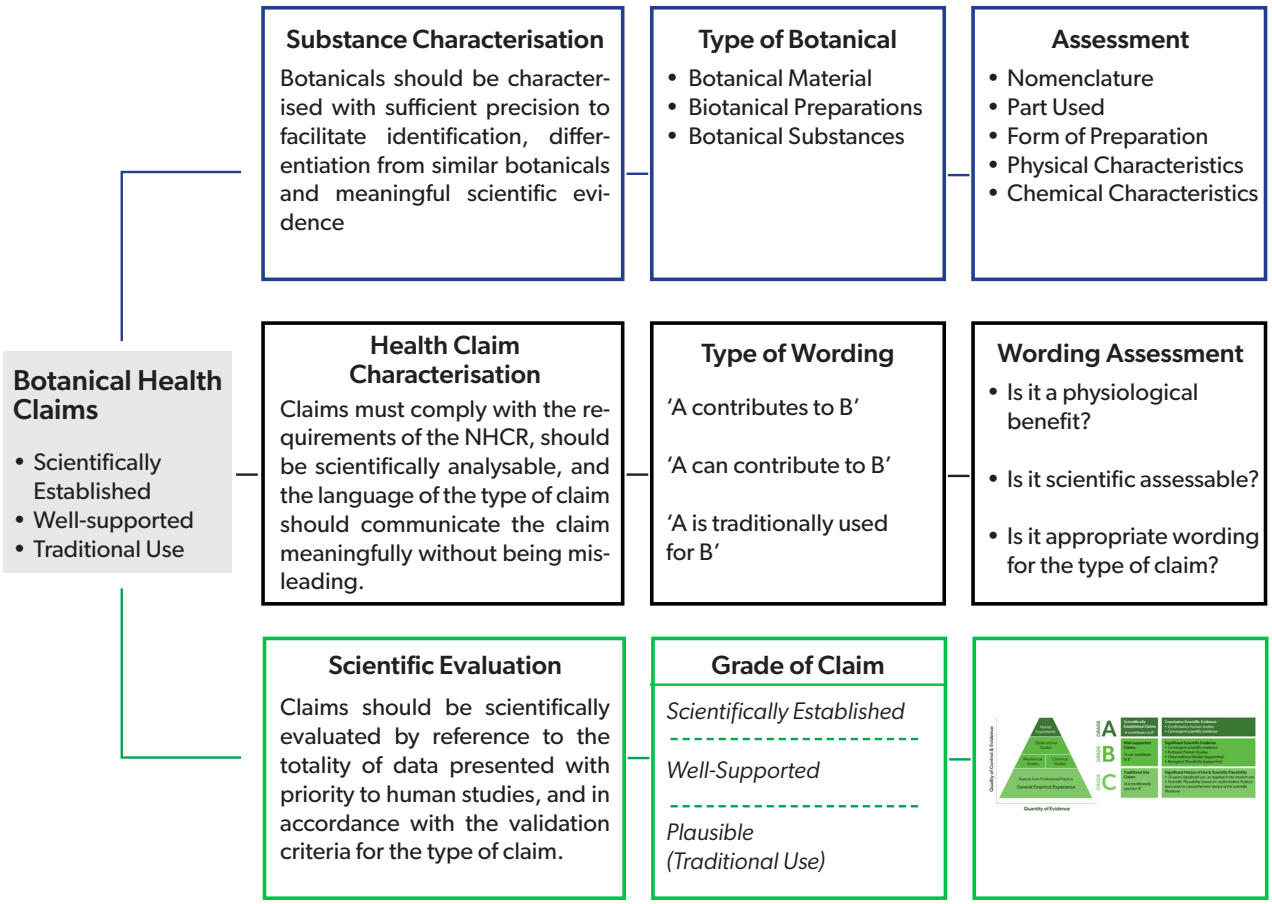
i. Botanical Health Claim Grade A (scientifically established).
   Level Ia evidence rarely exists today for botanicals used in food supplements; therefore the standard adopted is Level Ib – at least one conclusive randomised controlled trial and by another convergent human study of Level II evidence[12] on a similar or equivalent botanical preparation;
ii. Botanical Health Claim Grade B (well-supported).
   A convergent body of evidence is required, including at least one Level 1b study with bias or one controlled study without randomisation (Level IIa), or other type of quasi-experimental study (Level IIb), and evidence from observational studies (Level III);
iii. Botanical Health Claim Grade C (traditionally used).
   a. The existence of a tradition should be established by history of use evidence;
   b. Claims should be substantiated by Grade IV evidence (expert consensus publications) and/or by independently demonstrating scientific plausibility through a comprehensive review of the scientific literature[13].

[12] Note that the GRADE system itself does not require Level 1a evidence for Grade A claims substantiation; also, for many botanicals the convergent body of supportive evidence is extensive and significant.
[13] See R. Anton and Al, Traditional Knowledge for the Assessment of Health Effects for Botanicals – A Framework for Data Collection

4. THE EVALUATION OF BOTANICAL HEALTH CLAIMS

4.1 In its initial implementation of the NHCR, EFSA applies a systematic approach to evaluation based on Substances Characterisation, Assessment of the Wording of the Claim and Scientific Evaluation of the data presented. This approach is also applicable to the graded botanical health claims identified herein (see Diagram 2 below).

Diagram 2: The Systematic Evaluation of Botanical Health Claims



4.1.1 As with any objective analytical procedure of this nature, data should be sourced, recorded and reported on to a recognised, systematic format and in an open and transparent way. This is particularly important where the evaluation requires a comprehensive review of the scientific literature (see Data Collection Module: Appendix I).

4.2 Characterisation of the Botanical

4.2.1. General Principle

Botanicals should be characterised with sufficient detail to allow for precise identification, clear differentiation from similar botanicals, and meaningful scientific evaluation, taking into account the need to identify any specific characteristics of a botanical considered to be responsible for a claim.

4.2.2 Botanical preparations or substances should be defined as described in the EFSA General Scientific Guidance for Stakeholders on Health Claim Applications (Jan 2016) @7.1.1:

- The scientific (Latin) name (full systematic species, name including botanical family, genus, species, variety, subspecies, author's name and chemotype, where relevant; *e.g.* Punica granatum L, Lythraceae (Punicaceae));
- The part used (*e.g.* fruit, root, leaf, seed);
- Complete specifications of the manufacturing process (*e.g.* dried, hydro-alcoholic extraction, plant extract ratio) and how the product is standardised (*e.g.* by its content of one or more specific constituents).

4.2.3 Detailed information on the quality standards applied to botanical food supplement industry are also available in the EHPM Quality Guide for Food Supplements (see EHPM website[1]).

4.3. Evaluation of the Wording of Botanical Health Claims

4.3.1 General Principles Applied

Claims must be bona fide health claims in the context of the NHCR, they should be characterised so as to be amenable to scientific evaluation, and the language used should logically reflect the evidence assessed in a way that is clearly intelligible to the consumer:

- The wording of Botanical Health Claims should conform to the general principles of the NHCR, including referring to a beneficial nutritional or physiological effect in the forms defined in the legislation (see section 4.3.2.iii);
- The wording should be scientifically assessable (EFSA Guidelines 7.2.1);
- The wording of the claim should logically reflect the evidence evaluated and be clearly intelligible to the consumer.

4.3.2 Conformance with the Principles of the NHCR

i. Botanical health claims should not be false, ambiguous or misleading (Article 3.a); they should be truthful, clear, reliable and useful to the consumer (Preamble 29); and the beneficial effects as expressed in the claim should be easily understandable by the average consumer (Art 5.1.2).
ii. The claim should refer to a beneficial nutritional or physiological effect (Art.5.1a);
iii. Health claims may either refer to disease risk reduction, or to children's development, or to other functions specified below:
    a. The role of a nutrient or other substance in growth, development and functions of the body;
    b. Psychological and behavioural functions;
    c. Without prejudice to Directive 96/8/EC, slimming or weight control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet (Article 13).

4.3.3 Scientific Assessability of Functional Claims (EFSA Guidelines 7.2.1)

i. The claim should not be general nor non-specific (*e.g.* claims referring to general health and general well-being, or unspecified functions of organs or tissues are not permitted)[14];
ii. The claim should refer to a specific, beneficial physiological effect, defined as 'the mainte-

[14] However, general wording may be used on the face of a product, provided the full statement of claim is clearly stated elsewhere on the labeling: *e.g.* 'stated claim on the front 'Supports Digestion'; full claim on the label 'botanical 'a' is traditionally used to support thehealth of the digestive system by stimulating the release of digestive enzymes.'

nance, reduced loss or improvement of a body function';

4.3.4 The Wording of Scientifically Established Health Claims (Grade A)

The phrase 'contributes to' in a health claim, or action verbs such as 'reduce, decrease, improve', are used to communicate that the health benefit has been scientifically established; it is considered reasonable to assume that a majority of appropriately-informed people would understand this from the wording and that they would also understand that the contribution to health is to be expected.

4.3.5 The Wording of Well-Supported Health Claims (Grade B)

The phrase 'can contribute to', or similar wording,[15] in a health claim is used to communicate that, in the context of all consumers, the claim is supported by significant, but not conclusive scientific evidence; it is reasonable to assume that a majority of people would understand this from the wording and that they would also understand that the botanical has the potential to provide the benefit claimed, but does not necessarily do so;

4.3.6 The Wording of Traditional Use Health Claims (Grade C)

The phrase 'traditionally used to', or equivalent, in a health claim is used to communicate that there is a tradition of use; it is reasonable to assume that a majority of people would understand this from the wording, that they would expect a tradition to be in existence for at least one generation[16], and that they would also expect that a claim, which has been authorized, would be at least consistent with current understanding (i.e.be scientifically plausible).

Table 2a: Grading of evidences according to GRADE Group 2004

<table>
<tr><th>Level</th><th>Type of Evidence</th><th>Type of Study</th><th>Grade A Claim
Scientifically established
('contributes to, reduce decrease, improve')</th><th>Grade B Claim
Well supported
(can contribute)</th><th>Grade C Claim
Traditional
(traditionally used)</th></tr>
<tr><td>1b
IIa</td><td>Human
Experimental</td><td>RCT (fully randomised)</td><td>2 convergent studies with at least 1 RCT on the preparation</td><td rowspan="2">Convergent body of evidence, including at least 1 x clinical controlled study or other type of quasi-experimental study</td><td rowspan="4">Should be identified and reviewed as part of the overall evidence mix, in the absence of, or complementary to published meta-analyses or monographs</td></tr>
<tr><td>Significant experimental studies with varied randomisation and control</td><td rowspan="4"></td></tr>
<tr><td>IIb</td><td>Human
Quasi-Experimental</td><td>e.g. Not randomised clinical trials</td></tr>
<tr><td>III</td><td>Human
Observational</td><td>e.g. Cohort, Case Control,Cross- Sectional</td><td rowspan="2">Also reviewed as part of the overall evidence mix</td></tr>
<tr><td></td><td>Other (e.g. case histories, consumer satisfaction tests)</td></tr>
<tr><td>IV</td><td>Expert Consensus</td><td>Experts committee reports or experts opinions</td><td></td><td></td></tr>
<tr><td rowspan="2"></td><td rowspan="2">Mechanistic
(Human, animal or in vitro)</td><td>Mode of Action</td><td rowspan="3"></td><td rowspan="3"></td><td rowspan="3"></td></tr>
<tr><td>Bioavailability</td><td>As appropriate</td><td>As appropriate</td><td>As appropriate</td></tr>
<tr><td></td><td>Chemical Profiling</td><td>Precise Characterisation, including markers or actives</td><td>Required</td><td>Required</td><td>Required</td></tr>
<tr><td rowspan="4"></td><td rowspan="4">History of Use</td><td>Authoritative Publications</td><td rowspan="4"></td><td>Supportive</td><td>Preferred</td></tr>
<tr><td>Professional Writings</td><td rowspan="3"></td><td rowspan="3">As appropriate</td></tr>
<tr><td>Industry Sales Data</td></tr>
<tr><td>General Bibliography</td></tr>
</table>

4.3.7 Note that the final decision on the wording of an authorised claim is made at the end of the evaluation process on the basis of the evidence submitted and may not conform to the wording originally proposed.

4.4.1 The Evaluation of Grade A Claims on the basis of generally accepted Science

Botanical health claims using the words 'contributes to', or wording with an equivalent meaning, are evaluated on the basis of 2 convergent, human studies, with at least 1 conclusive randomised controlled trial on the specific preparation (Level 1b);

i. The RCT can only support a Grade A claim if:
   - The botanical preparation is sufficiently described;
   - The primary evaluation criteria relate to what is specifically being studied;
   - In the case of composite primary criteria, the criteria must be consistent;
   - The statistical methodology is detailed and reliable (viz. details of the analyses used);
   - The clinical relevance of the results are verified;
   - The results are obtained by comparing the actual group studied with a placebo group (not by referring to the starting baseline);

ii. "Negative" studies are taken into account in the assessment, if they meet the above criteria.

iii. Non-randomised trials, observational studies, and/or mechanistic studies may form part of the supporting evidence.

iv. The Botanical preparation must be precisely characterised.
   The claim must necessarily relate to a specific part of a specific vegetative organism, a specific type of preparation and specific conditions of use. Data on similar botanicals can be provided as background information, but to be of value as evidence of use/functionality, equivalence considerations need to be taken into account.

v. More conclusive evidence is not considered necessary.
   It is recognised that convergent evidence from meta-analysis of randomised, controlled trials, as currently relied on by EFSA, does establish scientific consensus of proof. The lesser standard is proposed for a number of reasons:
   - Apart from very few exceptions, the higher requirement for clinical research simply does not exist for botanicals today;
   - Because botanical preparations are complex matrices whose composition varies from one batch to another and depending on the production processes, existing clinical publications rarely properly describe the plant preparation studied;
   - It is considered the 'contributes to' claim appropriate reflects the evidence, if there is a well-conducted RCT and another well-conducted confirmatory trial.

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[15] Examples of alternative wording are 'can help', 'emerging science suggests … can/may'.
[16] One generation is taken to be 25 years as per the Anton et Alia paper referenced in note 13.
[17] *e.g.* 'a can help b'; 'emerging science suggests 'a' can contribute to 'b'
[18] *e.g.* The chemical profile of a botanical contains substances that may produce the claimed benefit;
The botanical contains specific compounds with a relevant mode of action;
Case histories from professional practice consistently show the defined benefit;
Observational studies show a benefit in a specific cohort of individuals consuming the botanical;
Experimental studies show the botanical can produce the benefit in certain circumstances.

4.4.2 The Evaluation of Grade B Claims on the basis of Well-Supported Science

Botanical health claims using 'can contribute to', or wording with equivalent meaning[17], are evaluated on the basis of a convergent body of evidence[18], including at least one well conducted, controlled study without randomisation, or positive, but not-conclusive RCT, or other type of quasi-experimental study. Observational studies, expert reports and opinions and mechanistic studies form part of the supporting evidence.

i. The claim should relate to a specific part of a specific vegetative organism, a specific type of preparation and specific conditions of use. Data on similar botanicals can be provided as background information, but to be of value as evidence of use/functionality, equivalence considerations need to be taken into account.

ii. This approach has the advantage of taking account observational studies, including extensive use in well-conducted professional practice, reflecting the use of the botanicals in real life.

4.4.3 Evaluation of Grade C Claims on the basis of Traditional Use and Scientific Plausibility

i. Where possible the claim should relate to a specific part of a specific vegetative organism, a specific type of preparation and specific conditions of use. Data on similar botanicals can be provided as a background, but if this is to be used as evidence of use or functionality, equivalence considerations need to be taken into account.

ii. Establishing the Tradition of Use.
It is a requirement of the evaluation of the wording of a traditional use claim that the existence of a tradition of use for one generation or more (*e.g.* 25 years[16]) should be demonstrated. It is important that the tradition be quantitatively and qualitatively identified as extensively as is practically possible through authoritative publications and/or data that has been independently collated because the validity of a tradition is initially established by the strength of the history of use[19]:

- Qualitatively, data should be differentiated into general bibliographic data, commercial data and data relating to professional use; data from professional use is of particular significance because case-studies from well-conducted professional practice are a form of observational data of scientific significance;

- Data should be quantified by reference to volume of use and duration.

There is no hard rule governing the significance of history of use data, but it is self-evident that strong traditions of use that are growing in popularity are more credible than limited traditions of use that are in decline.

Claims that have evolved in the modern era in response to modern experience and science, or to botanicals that have similarly evolved, may be considered traditional, provided they still

[19] Cf. EMA Guidelines for Traditional Herbal Medicines: EMA/HMPC/104613/2005 – Rev. 1. Sept 2017

An indication 'exclusively based upon long-standing use' may be plausible, even if no supporting scientific data are available. Evidence on the consistent use should include a well-defined posology (for specific age groups if available), administration form and indication. If a traditional herbal medicinal product has long fallen into disuse, this might indicate that in practice the efficacy of the traditional herbal medicinal product is not plausible.

refer to substantively the same health benefit or botanical; the evolution of the claim should be described and differences defined and rationalised.

iii. Establishing Scientific Plausibility.
Scientific plausibility is established by **authoritative publications** (*e.g.* recognised Monographs) and/or by a **comprehensive review of the scientific literature**. The evidence in support of plausibility includes the nature and extent of the history of use, studies of the action of substances identified in the chemical profiling of the botanical, observational studies and experimental studies – human or otherwise.

Because authorisation of a traditional use claim must include a review of its scientific plausibility, it is essential that data supplied is a balanced reflection of a comprehensive review of the scientific literature. To ensure this is the case, data should be sourced, collated and reported on in a transparent way, using a standard classification of the types of data, and ideally **a recognised data collection model** (*e.g.* Appendix I).

Traditional health claims are based on observed or evaluated health benefits in humans and not on biological or mechanistic evaluation criteria that, by definition, are not traditional. However, if available, **biological evidence on the mechanism of action** should be provided to support the plausibility of the traditional experience, or to explain modifications to the tradition in the modern generation.

Guidelines, Monographs or other publications, if recognised as authoritative, can be taken as reflecting a comprehensive and balanced review of specific bodies of evidence; as such they replace the need for independent data collection and review.

5. Conclusions

The Nutrition and Health Claims Regulation, as currently implemented, is not an appropriate response to the challenges presented by the evolving understanding of the nature of food and its effects on human health. The protection of consumers from being misled has been prioritised over the rights, needs and aspirations of consumers for information. This has resulted in an excessively restrictive regulation that is inhibiting both authentic commercial activity, and research and development, causing functional products to be placed on the market without any indication as to their safe and effective use, and inducing consumers to seek information on their own initiative from uncontrolled sources—all of which activities increase the risk of consumers being misled. The situation is compounded by reliance on a medical model of scientific research to evaluate the isolated action of individual food components on human physiology—an approach with limited application to the health benefits of foods.

This paper seeks to address these deficiencies by re-prioritising the need to facilitate informed consumer choice and by developing scientific assessment methodologies, which reflect the long term, iterative nature of scientific inquiry into the nature of foods and their effects on human health. The paper shows that it is possible to grade botanical health claims from the plausible to the certain, to evaluate these claims by reference to specified levels of evidence and to use qualified

language to communicate the outcomes of these evaluations to consumers in a way that is useful, honest, accurate and meaningful. This approach logically involves dealing with uncertainty, but, the methodology proposed shows that this can be achieved without compromising the required stringency.

The development of the Nutrition and Health Claims Regulation along the lines suggested is essential to the Health Products industry, and in particular to the food supplement sector, because the integrity of the industry depends on being able to communicate the actual or potential health benefits of foods to consumers who are interested in taking personal responsibility for their health. However, given that all foods have an immediate effect on body function with longer term implications for health, the approach could also significantly benefit all consumers and the food industry as a whole. Importantly, unlike the current situation, this is an approach which could attract wide-spread industry support, and which, as such, is capable of creating the virtuous circle of successful research/successful commercialisation, which is in the interest of all stakeholders.

This paper has concerned itself solely with health claims in the context of the Nutrition and Health Claims Regulation (EC/1924 2006). Quality issues have only been addressed in so far as they are required for claims evaluation, and safety issues have not been addressed at all. In reality, however, quality, safety and claims substantiation are managed in an integrated way by the food supplement industry as part of the product development process. Detailed information on the quality standards that need to be applied to foodstuffs produced for their nutritional and physiological effects is provided in the EHPM Quality Guide for Food Supplements, available on the EHPM website[1].

When considering how such an approach might be legislated for, the key issue is the interpretation of the term 'generally recognised science' as used in the NHCR. If this is taken to allow only simple statements of fact based on scientific consensus of proof, it is difficult to see how the EHPM proposals could be implement other than by new legislation; if, a more liberal approach is adopted to the term and its implication, it would be possible to facilitate the EHPM proposals either by amending the NHCR as deemed appropriate and issuing new implementing regulations, or, by just issuing new implementing regulations on their own. These changes could be introduced either in the context of Food Law in general to cover all foods, or they could be implemented initially just in the context of food supplements through an amendment to the Food Supplements directive.

About EHPM

EHPM was created in 1975 and represents 1600 health-product manufacturers in 14 European countries. Through our member associations, EHPM aims to provide consumers with safe, science-based, high quality products as well as accurate and helpful information about their nutritional value and use, and to assure a fair European regulatory framework for the food supplement sector.

For more information on the proposal please contact the EHPM Secretariat:
Rue des Colonies 56, B-1000 Brussels, Belgium
info@ehpm.org

Appendix I Data Collection Module

The methodology currently applied by EFSA to establish what in this document is referred to as Grade A claims ultimately depends on confirmatory clinical trials to establish consensus of proof. However, there still is a requirement to collate and present data in a transparent and systematic way (EFSA Guidance to Applicants @ 4.2.1).

In the case of Grade B and C claims, where conclusive human studies are not available, the conduct of a comprehensive review of the scientific literature and history-of-use becomes more important – and with this importance comes a greater need for a transparent and systematic approach to the searching, recording and reporting of data;

i. The data collection, search, recording and reporting policies and methodologies should be described,
ii. Literature sources should be specified:
    a. Guidance is needed on the literature that is considered authoritative;
    b. The literature searched and selection criteria should be recorded;
iii. A protocol should be established for Internet searches that includes:
    a. A description of the procedures followed;
    b. Exclusion/inclusion criteria in relation to the databases searched;
    c. Identification of the databases searched;
    d. The search strategy (including terms used, limits used such as dates of publication, publication types, languages, population groups, default tags)
    e. Search techniques;
iv. A common approach should be adopted to recording, presentation and collation of data, based on the defined outcomes sought, including exclusion/inclusion criteria applied to data recorded/omitted;

Presentation of Information on Authoritative Publications

	Publication Type	*Number of Publications*	*Studies Reviewed*
1	Existing Monographs		
1	Meta analyses (as available)		
1	Systematic Reviews of use in humans		
1	Guidelines, consensus papers, educational textbooks		
1	Professional Publications		
1	Systematic Reviews of Mechanism of Action		

Organisation of Data

(Adapted from EFSA Guidance to Applicants @ 4.2.1)

Level of Evidence		Partici-pants	Studies Identified	Studies Excluded
	Human Experimental Studies			
Ib	Randomised controlled studies			
IIa	Controlled, not randomised			
	Sub-Totals			
IIb	**Quasi-Experimental Studies**			
	Observational studies			
	Other quasi-experimental studies (specify)			
	Sub-Totals			
III	**Human Observational Studies**			
	Cohort Studies			
	Case Control Studies			
	Cross Sectional Studies			
	Case Histories from Professional Practice			
	Other Observational studies (specify)			
	Sub-Totals			
IV	**Evidence of expert committee reports or expert opinion**			
	Mechanism studies			
	Human studies			
	Animal studies			
	In Vitro			
	Sub-Totals			
	Chemical Profiling			
	Quality Profiling (including markers)			
	Active ingredient profiling			
	Sub-Totals			
	History of Use Data			
	Reports from professional practice			
	Commercial Data			
	Other history of use data			
	Sub-Totals			