

*The Scientific Substantiation of
Health Claims:
A Global Assessment*

Resource Centre | Health supplements

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New Delhi, 1st May 2018

Outline

- ✿ A renaissance for food biosciences, research and product innovation
- ✿ The regulatory frameworks for nutrition & health claims in Codex Alimentarius and EU
- ✿ Scientific substantiation of health claims
- ✿ Role of the European Food Safety Authority (EFSA)
- ✿ Consumer understanding of health claims
- ✿ Challenges facing researchers and legislators

The aims of the global legislation on Nutrition and Health Claims

- Achieve a high degree of consumer protection—to eliminate false and misleading claims.
- Ensure confidence in claims on foods by requiring that all health claims are scientifically substantiated.
- Promote and protect innovation.
- Improve free movement of goods and ensure fair competition

(Codex Alimentarius Commission)

Consumer understanding

Health claims

- ◆ Help consumer understanding of role of food and food constituents in maintaining and improving human health and in reducing the risk of major diseases (e.g. cardiovascular disease, type 2 diabetes, certain cancers, osteoporosis).
- ◆ Educate consumers so that they may make informed choices about the beneficial effects as expressed in the claim.

Codex Alimentarius Commission

Globally, the structure and process for scientific substantiation and authorisation of health claims is based mostly on the principles and guidelines set out by the Codex Alimentarius Commission.

- General guidelines on claims CAC/GL 1-1979
- Guidelines for use of nutrition and health claims CAC/GL 23-1997 (adopted 1997; revised and amended 2001–2013)

Annex adopted in 2009 on Recommendations on the scientific substantiation of claims

Codex Guideline: CAC/GL 23-1997

Using Codex as a reference point, regulatory frameworks for nutrition & health claims are converging and becoming more similar around the world.

- ❑ Nutrient function (Section 2.2.1)
- ❑ Other function (Section 2.2.2)
- ❑ Reduction of disease risk (Section 2.2.3)

The creation of a harmonised, scientifically robust, transparent and proportionate framework for the assessment of health claims is a critical regulatory and policy issue.

Codex Alimentarius

Scientific substantiation of health claims

- ◆ Identification of the proposed relationship between the food or food constituent and the beneficial physiological effect.
- ◆ Identification of relevant valid measurements and biomarkers for the claimed beneficial effect.
- ◆ Evaluation of the totality of the available relevant scientific data, weighing the evidence across studies and determination if, and under what circumstances, a claimed relationship is substantiated.

Codex Alimentarius

From the systematic review of the scientific evidence establish:

The quantity of food/pattern of consumption required to obtain the claimed effect can reasonably be consumed within a balanced diet (as relevant for the target population for which the claim is intended).

What is the totality of the available scientific data?

- Human intervention/efficacy studies, randomised controlled trials (RCTs) including use of validated biomarkers
- Human observational/epidemiological studies
- National/international expert consensus reports, including authoritative statements
- Animal and *in vitro* studies (supportive evidence of mechanism)
- Traditional knowledge and history of use

Codex Alimentarius

Sources of high quality, consistent and biologically plausible scientific evidence include:

- **For nutrient function claims**—based on generally accepted authoritative expert scientific bodies that have been verified and validated over time.
- **For a food category** —based on observational evidence such as epidemiological studies.

European classification of claims on foods



Nutrition claims

- nutrient content
- comparative
- 'other substance'

Annex

Health claims

Based on generally accepted scientific evidence

Article 13.1

Based on newly developed scientific data/IPR protection

Article 13.5

Reduction of disease risk and claims referring to children's development and health

Article 14

Regulation (EC) No 1924/2006, Regulation (EC) No 353/2008

Article 2 (5)

“Health claim” means any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health.

Article 2 (6)

“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 for the development of a human disease.

Article 13: Health claims other than those referring to the reduction of disease risk and to children's development and health

- Role of nutrient or other substance in growth, development and the functions of the body
- Psychological and behavioural functions
- Slimming, weight control, reduction in sense of hunger, increase in satiety or reduction of available energy

Commission Regulation EC No 353/2008 of 18th April 2008 establishing implementing rules for applications for authorisation of health claims as provided for in Article 15 of Regulation 1924/2006

- Each application shall cover only one relationship between a nutrient or other substance, or food or category of food and a single claimed effect.
- Sets out structure of the application (consistent with EFSA Scientific and Technical Guidance).

Official Journal of the European Union, 19th April 2008

EFSA Revision 2 scientific & technical guidance for the preparation and presentation of a health claim application

EFSA J. 2017; 15(1): 4680

- PART 1: Administrative and technical data
- PART 2: Characterisation of the food/constituent
- PART 3: Characterisation of the claimed effect
- PART 4: Identification of pertinent scientific data
- PART 5: Overall summary of pertinent scientific data
- PART 6: Annexes to the application

Appendices:

- A. Application form (mandatory)
- B. Summary of the application
- C. Information to be presented in a full study report for unpublished studies or for proprietary studies

Synopsis of pertinent scientific data

- **Identification of the study**: authors, article title, affiliations, declaration of interests, source of funding, ethical approval, objectives
- **Report status**: published, accepted for publication, unpublished
- **Literature search and other data sources**
- **Verification of study eligibility**: meets inclusion/exclusion criteria
- **Description of the study group**: age range, sex, ethnicity, inclusion/exclusion criteria, geographical region, biological appropriateness to target population
- **Outcome measures/results/statistical significance**
- **Study quality**: power calculations, validated biomarkers

EFSA NDA Panel assessments

Consider the extent to which:

- The food/constituent is defined and characterised
- The claimed effect is defined and has a beneficial nutritional or physiological effect ('beneficial to human health')
- A cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use)
- The quantity of food/pattern of consumption required to obtain the claimed effect can reasonably be consumed within a balanced diet

Reference: [Technical Report of EFSA: *EFSA Journal* \(2009\) 7 \(11\): 1386](#)

EFSA Guidance Documents 2011 to 2018

Scientific requirements for health claims

- Immune system, the gastrointestinal tract and defence against pathogenic micro-organisms
- Antioxidants, oxidative damage and cardiovascular health
- Appetite ratings, weight management and blood glucose concentrations
- Bone, joint, skin and oral health
- Nervous system, including psychological function
- Physical performance

Reasons for rejection by EFSA

- The foods/food constituents were not sufficiently characterised.
- Effects of food matrix, processing & stability information, bioavailability & content variability not sufficiently characterised
- Conclusive evidence of a cause and effect relationship was not established between the food/food constituent & the claimed effect.
- Lack of systematic literature review and no specific inclusion/exclusion criteria
- Criticism of study designs, absence of power calculations, insufficient information on background diet & lifestyle, failure to describe target group, intervention trials lacking, no lowered risk factor/no measurable effect
- Patient (clinical studies) not used as evidence for health effects in general population
- Claims considered to be medicinal (prevention, alleviation, cure)

EU Register of authorised nutrition and health claims at: <http://ec.europa.eu/nuhclaims>

Permitted claims are:

- Based on and substantiated by generally accepted scientific evidence (EFSA/European Commission)
- Permitted only if the average consumer can be expected to understand the beneficial effects as expressed in the claim

Regulation (EC) No 1924/2006



Process for the Assessment of Scientific Support for Claims on Foods

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PASSCLAIM

A European Commission (EC) Concerted Action
organised by International Life Science Institute -
ILSI Europe

Aggett P *et al.* (2005) *Eur J Nutr* **44** (1), 1-30

Insufficient

Possible

Probable

Convincing

In vitro or animal studies only

Small uncontrolled human studies

Epidemiological data with contradictory results

Single small human study

Epidemiological data with consistent results

+ Difficulty measuring
+ contradictory lab data

Single large human study

+ contradictory epidemiological data

Multiple small human studies

+ consistent results with flawed designs

Meta-analysis

+ supportive laboratory data

+ biological plausibility and consistent lab data

+ supportive epidemiological data

+ consistent results with good designs

Critical reviews by experts

Evidence accepted by scientific bodies or independent expert bodies

e.g. Judgements by government-related organisations (EFSA, FDA, AFSSA, ...)

e.g. Judgements by expert organisations (WHO, SACN, NAS, ...)

e.g. Judgements by scientific organisations (ESPGHAN, ...)

e.g. Recent acknowledged text books

e.g. Monographs (ESCOP, ...)

History of use

1

2

3

4

5

Emerging Evidence

Significant Scientific Agreement

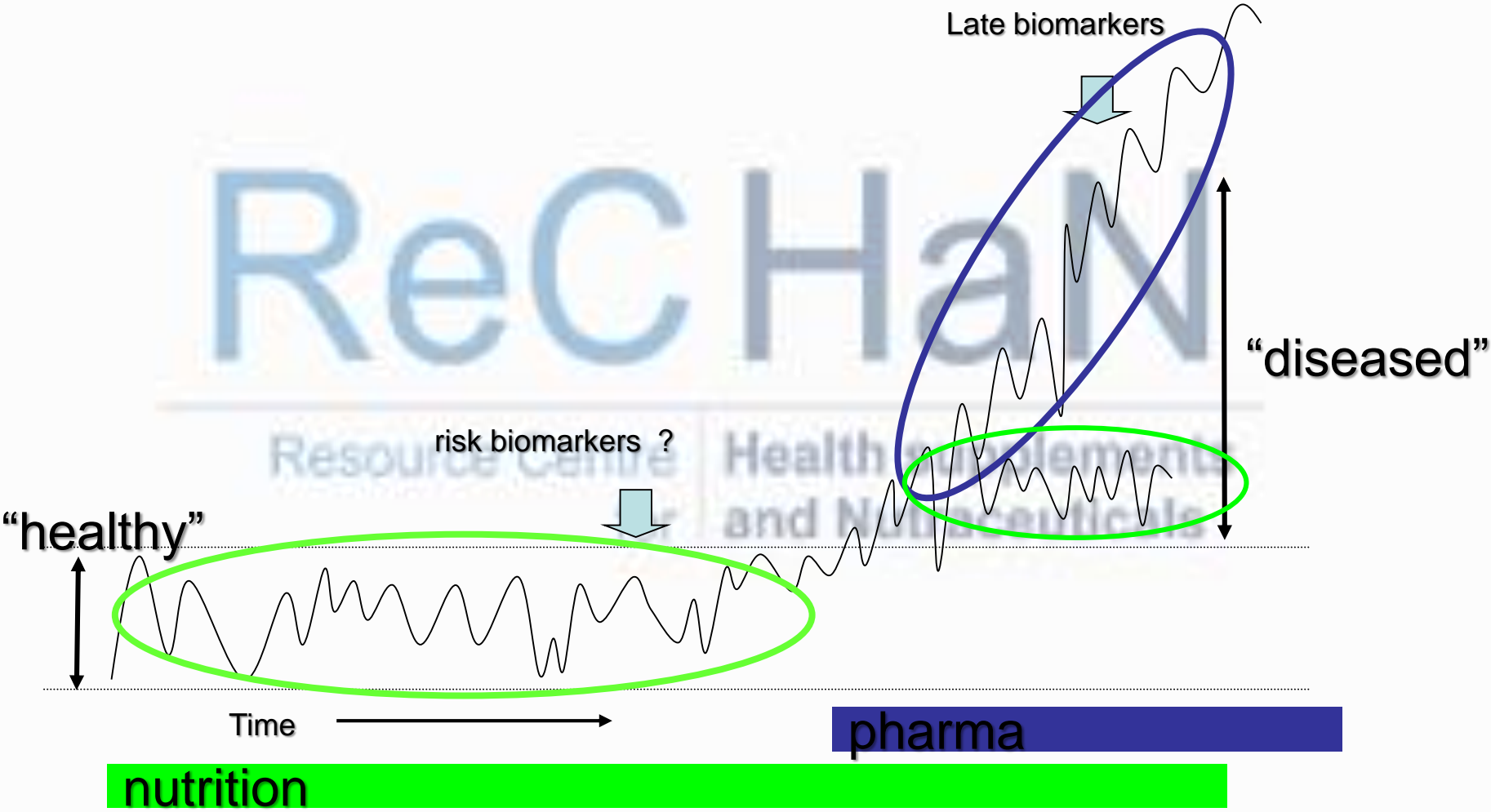
Consensus

Too few biomarkers

- LDL-cholesterol
- Blood pressure
- Colon polyps
- Bone mineral density, fracture
- Blood sugar/insulin resistance
- Cognitive decline

(Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease (2010) IOM provides a transparent and consistent framework for analytical validity and evidentiary qualification.)

From “healthy” to “diseased”: disturbing homeostasis



PROCLAIM identifies limitations of RCTs in evidence-based nutrition (EBN)

The success of RCTs in evaluating medical treatments has blinded nutritionists, regulators and editors to the fact that it is a method ill suited to the evaluation of nutrient effects.

- Drugs are intended for, and evaluated in, sick people.
- Foods and food constituents, nutritional recommendations and health claims are first of all for well people.
- The response to a drug is typically evaluated relative to its absence.
- The few validated biomarkers are developed for diseases, not adaptive responses in healthy people.
- Nutritional effects manifest themselves in small differences over long periods of time.
- Homeostatic mechanisms keep physiology within an individual's normal range.

Gallagher AM *et al.* (2011) *Brit J Nutr* **106** (Suppl S2), S16–S28

Examples of health claims related to cardiovascular health

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Cardiovascular health

EFSA J 2011; 9(12): 2474; EFSA J 2018; 16(1): 5136

Beneficial physiological effects include:

- Maintenance of normal or reduction of LDL cholesterol concentration
- Maintenance of normal HDL cholesterol concentration as long as LDL cholesterol concentration is not increased
- Maintenance of normal arterial blood pressure
- An improvement in specific endothelial functions (e.g. endothelial-dependent vasodilation) during sustained exposure to the food/constituent
- Maintenance of the elastic properties of the arteries
- Decreasing platelet aggregation in subjects with platelet activation during sustained exposure to the food/constituent
- Maintenance of normal venous blood flow
- Maintenance of normal homocysteine metabolism

Heart-related examples of well-established nutrient function claims authorised under Article 13 of the Nutrition and Health Claims Regulation 432/2012/EU

Vitamin C	Contribute to the protection of cell constituents from oxidative damage
Vitamin E	
Selenium	
Zinc	
Thiamin (vitamin B1)	Contributes to the normal function of the heart
Folate	Contributes to normal homocysteine metabolism
Magnesium	Contributes to muscle function including heart muscle
Potassium	Helps maintain normal blood pressure

Examples of applications for health claims for cardiovascular benefits given favourable EFSA opinions include:

- Plant sterols and plant stanol esters and low/reduced blood cholesterol
- Danacol[®] low fat dairy product and low/reduced blood cholesterol
- Cocoa flavanols and maintenance of normal endothelial-dependent vasodilation

Omega-3 fatty acid health claims

Claims approved by EFSA include:

- **EPA/DHA** heart
Contributes to the normal function of the heart (250 mg EPA and DHA/day)
- **EPA/DHA**
Contributes to maintenance of normal blood pressure (3 g EPA and DHA/day)
- **DHA**
Contributes to maintenance of normal brain function & normal vision (250 mg DHA/day)
- **DHA**
Contributes to normal brain development of the foetus & breastfed infants (200 mg DHA for pregnant & lactating women in addition to 250 mg EPA and DHA/day)

YES: EFSA scientific opinion on Article 14 health claim related to oat beta-glucan and lowering blood cholesterol and reduced risk of heart disease

- Application from CreaNutrition AG, Switzerland
- Oat beta-glucan is sufficiently characterised.
- Lowering blood LDL cholesterol concentrations is a beneficial physiological effect by decreasing risk of CHD.
- Foods should provide at least 3 g of oat beta-glucan per day.
- The target population is adults who want to lower their blood cholesterol concentration.
- Substantiation based on 3 meta-analyses with 12, 25 and 18 studies.

EFSA Journal (2010) **8** (12), 1885

YES: EFSA scientific opinion on Article 13.5 health claims related to water-soluble tomato concentrate (WSTC) and platelet aggregation

- Application from PROVEXIS NATURAL PRODUCTS LTD on Fruitflow[®]
- WSTC is lycopene free, fat free, low sugar; 37 constituents identified to show inhibition of platelet aggregation. WSTC is sufficiently characterised.
- Maintenance of normal platelet aggregation is beneficial to health.
- Achievement of claimed effect, 3 g WSTC I or 150 mg WSTC II in up to 250 ml of fruit juices, flavoured water or yogurt drinks
- Substantiation based on 3 published studies (all RCTs) and 5 unpublished human studies (including 3 RCTs).

EFSA Journal (2009) **1101**, 1–15

Provexis Natural Products Ltd —Fruitflow®

Article 13.5 health claim: on the beneficial effect of water-soluble tomato concentrate (WSTC)

■ Applicant's proposed wording

“Helps to maintain a healthy blood flow and benefits circulation”.

■ EFSA comments (*EFSA Journal* (2009)1101, 1–15)

The following wording reflects the scientific evidence: “Helps maintain normal platelet aggregation”. “Blood flow” and “healthy circulation” do not reflect the scientific evidence.

■ European Commission Decision, 17th December 09

WSTC helps maintain normal platelet aggregation, which contributes to healthy blood flow.

Consumer understanding

- Health claims are permitted in the EU only if the average consumer can be expected to understand the beneficial effects as expressed in the claim.
- Average consumer means the consumer who is reasonably well informed and reasonably observant and circumspect, taking into account social, cultural and linguistic factors.

What do we know about consumers and health claims?

- Seen as useful and helpful to make healthier choices
- Can take years of exposure for the claimed diet/health relationship to become familiar
- Consumers are sceptical about commercial health claims
- Dislike long, complex and scientifically worded claims

“KISS”

Keep It Soft and Sentimental

ReC Han

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**Keep It Serious and
Scientific**

Challenges to researchers

- Identification and validation of relevant biomarkers that can detect early signs of homeostatic disturbance and/or predict potential benefits relating to maintenance or improvement of a function and those associated with reduced risk of disease
- The strengths and limitations of different sources of evidence (e.g. randomised controlled trials/human intervention studies, epidemiological prospective cohort studies, *in vitro* & animal studies, history of use)
- Methodologies for the assessment of the totality of the available data and the development of a scientific framework for weighing the strength, consistency and biological plausibility of the evidence
- Consumer understanding research to link the totality of the available data and weight of evidence to claims that are truthful and meaningful to consumers

Challenges to legislators

Legislation

- Extent to which a cause and effect is demonstrated (convincing, probable, possible, insufficient)
- The claimed effect must be a beneficial nutritional or physiological effect.
- Requires weighing of evidence by assessing the strength, consistency and biological plausibility (likelihood) of the totality of the available data.
- Categorise and present sources of data by scientific hierarchy.
- Proportionate approach
- Stimulate research & innovation
- Consumer protection/informed decisions

EFSA interpretation

- Conclusive evidence of cause and effect YES/NO
- The claimed effect must be a physiological effect using validated biomarkers.
- Application of PASSCLAIM as gold standard to be achieved: (PASSCLAIM set criteria against which state-of-the-art evidence could be transparently graded).
- Uses medicinal paradigms. Evidence-based medicine
- Rigid approach
- Likely to stifle innovation
- Scientific wording may undermine consumer understanding

Take home messages

- Codex Alimentarius provides the principles and guidelines for scientific substantiation and health claims
- Regulatory frameworks for nutrition and health claims are converging and becoming more similar around the world

Take home messages

- Scientific substantiation should take into account:
 - Generally accepted scientific evidence
 - The totality of the available scientific data and weight of evidence, and recognize the strengths and limitations of different sources of evidence

Take home messages

- Evidence based medicine (EBM) approaches are not always appropriate for scientific substantiation of health benefits of foods and food components
- Claims should be truthful and meaningful for consumers to reflect the strength of the evidence and biological plausibility of the food and health relationship

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