Scientific Substantiation of Health Claims on Foods in the EU

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Outline

- EU Regulation on nutrition and health claims – the need for substantiation
- EFSA review of the evidence for scientific substantiation of health claims
- Health claims with a favourable evaluation by EFSA
- Issues arising with review of evidence on health claims by EFSA
- EFSA guidance for applicants for health claims
- Conclusions

EU Regulation 1924/2006 on Nutrition and Health Claims made on foods:

the requirement for scientific substantiation of health claims

EU Regulation 1924/2006 - features

- **Health claims include:**
  - disease risk reduction claims
  - function claims
  - claims on development and health of children
- Applies equally to foods and supplements
- All claims must be authorised and all must be assessed by EFSA before authorisation
- A single standard of evidence for substantiation of all health claims
- No provision for qualified health claims

EU Regulation 1924/2006: scientific substantiation

- Scientific substantiation should be the main aspect to be taken into account for the use of health claims and food business operators using claims should justify them

- Health claims should only be authorized for use in the Community after a scientific assessment of the highest possible standard

- In order to ensure harmonized scientific assessment of these claims, the European Food Safety Authority should carry out such assessments - independent review

EU evidence standard for health claims

- All claims must be substantiated by generally accepted scientific evidence, taking into account totality of available scientific data, and weighing the evidence

  = generally accepted by scientific experts

- May be considered similar to FDA Significant Scientific Agreement

EFSA review of the evidence submitted for scientific substantiation of health claims

EFSA's role in assessment of health claims

- EFSA's **NDA panel** performs **independent assessment** of claims and provides scientific advice on substantiation
  - 21 Panel experts
  - Supported by EFSA staff and additional experts (as needed)

Authorisation of claims is by EU Commission (+ EU Member States + Eur. Parliament scrutiny)

Main issues addressed by NDA Panel

1. is the food/constituent defined and **characterised** ?

2. is the claimed effect defined and is it a **beneficial physiological effect** ?

Defining the claim

3. is a **cause and effect relationship** established between the consumption of the food/constituent and the claimed effect?

- for the **target group**
- under the proposed **conditions of use**

Substantiation of the claim

Evidence review - steps

1. Selection of relevant human studies (central studies)
2. Review of individual human studies
3. Review of studies on biological plausibility - mechanisms, bioavailability
4. Weighing the evidence - combining the relevant human studies + other studies to conclude on substantiation

– transparent scientific judgement of the NDA Panel

– published scientific opinion in EFSA journal:

http://www.efsa.europa.eu/en/publications/efsajournal.htm

Relevant human studies

- studies carried out with the food/constituent for claim
- appropriate outcome measure(s) for the claimed effect
- conditions for studies comparable to conditions of use for claim (e.g. quantity of food/constituent)
- study groups representative of the target group or extrapolation to the target population possible

Review of relevant human studies

- Published and unpublished studies accepted
- Review by study type – e.g. intervention, observational
- Study quality – design, execution, analysis, reporting
- Additional information may be requested from the applicant
- Studies of low quality may be excluded

Weighing the evidence

- combine the relevant human studies by study type (RCT strongest evidence)
  - number of studies for and against, taking into account study population, study quality, study size, effect size, dose-response
  - consistency among studies
- evidence for biological plausibility – bioavailability, mechanisms
  - studies in humans, animals, *in vitro*

Communication with applicants

- For health claims submitted under individual authorisation procedures dialogue possible between EFSA and applicant during assessment

  - Dialogue with applicant is very important for EFSA assessment

Health Claims with a favourable evaluation by EFSA

Examples

Claims for development and health of children (11)

Claim	Food/constituent
Brain development + eye development in foetus, infant	DHA (maternal)
Visual development in infant	DHA (infant)
Growth & development of children Cognitive development	ALA, LA Iron

Iron and cognitive development

Authorized claim:

Iron contributes to normal cognitive development of children

EFSA:

Based on evidence of the biochemical functions of iron in the brain and effects of iron deficiency on cognitive function in children

Conditions of use:

The claim may be used only for food which is at least a source of iron (≥15% RDA per 100g)

Disease risk reduction claims (11)

Claim	Food/constituent
Blood LDL-cholesterol/heart disease	- Plant sterols/stanols - oat β-glucans - MUFA/PUFA replacing saturated fat
Dental plaque/caries Plaque acids/caries Demineralisation/caries	Sugar-free chewing gum
Bone density/osteoporotic fracture Falling/osteoporotic fracture	- Ca; - Ca + vitamin D - Vitamin D

Plant sterols/plant stanol esters and coronary heart disease

Authorized claim:

Plant sterols and plant stanol esters have been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease.

EFSA:

Claim substantiated based on 41 human studies (sterols) and 30 human studies (stanol esters)

Conditions of use: Information to the consumer that the beneficial effect is obtained with a daily intake of 1.5-2.4 g plant sterols/stanols

Function claims (>200)

Claim	Food/constituent
Tooth mineralisation	Sugar replacers, fluoride
Bone	calcium, vit. D, vit. K
Body weight	Meal replacements, VLCD
Bowel function	Cereal fibres (various)
Blood glucose after meals	Pectins, guar gum, resistant starch, sugar replacers
Blood pressure	potassium, reduced sodium
Blood LDL-cholesterol	Pectins, β-glucans, MUFA, PUFA, reduced sat. fat
Platelet aggregation	Water sol. tomato conc.

Nutrient function claim: calcium and bone

Authorized claim:

Calcium is needed for the maintenance of normal bones

EFSA:

Based on generally accepted function of calcium in bone

Conditions of use: The claim may be used only for food which is at least a source of calcium (≥15% RDA per 100g)

Water soluble tomato concentrate (WSTC) and blood flow

Authorized claim:

Water-Soluble Tomato Concentrate helps maintain normal platelet aggregation, which contributes to healthy blood flow

EFSA:

claim substantiated based on eight human studies and seven non-human studies (including 10 studies claimed as proprietary: 7 unpublished studies protected)

Nutrient function claim: calcium and bone

Authorized claim:

Calcium is needed for the maintenance of normal bones

EFSA:

Based on generally accepted function of calcium in bone

Conditions of use: The claim may be used only for food which is at least a source of calcium (≥15% RDA per 100g)

Issues arising with review of evidence on health claims by EFSA

Examples

Quality of human studies

Commonly observed sources of bias

Intervention studies

- design – insufficient size, control of confounding
- execution - randomisation, blinding
- statistical analysis - drop outs and treatment of missing data, treatment of multiple outcomes

Observational studies

- measurement of relevant exposure, confounding

Evidence from studies in patients

- Health claims are for general population, not treatment of patients (medicinal)
- Some diseased populations may be considered representative of (non-diseased) target groups when mechanisms for effect are the same in both groups

  - Type II diabetics (treated with diet only) - for claims on post-prandial blood glucose
    - But not if treated with drugs for lowering blood glucose

Study group not representative of target group for the claim

Claims on joint function:

- NDA Panel does not consider that findings from studies in osteoarthritis patients can be extrapolated to the general population

  - Response of joint tissues in osteoarthritis to exogenous substances may not be the same

Claims on probiotics/prebiotics

Non-authorised claim:

Helps to maintain a desirable balance of beneficial bacteria in the digestive system

- EFSA does not consider that increasing numbers of lactobacilli/bifidobacteria in the intestine is a beneficial physiological effect *per se*
- Beneficial consequences should be demonstrated
  - lactose digestion (claim authorised)
  - defence against pathogens in the intestine (no claim substantiated to date)

Live cultures in yoghurt and lactose digestion

Authorized claim:

Live cultures in yoghurt or fermented milk improve lactose digestion of the product in individuals who have difficulty digesting lactose

EFSA:

Claim substantiated based on human studies:

thirteen of fourteen human studies showed enhanced digestion of lactose in yoghurt in lactose maldigesters; also strong evidence of biological plausibility

EFSA Guidance for Applicants for Health Claims

EFSA Guidance for Substantiation of Health Claims on Foods in EU

- General guidance – principles for scientific substantiation of health claims
- Specific guidance on scientific requirements for specific types of health claims
- >400 scientific opinions, technical reports

http://www.efsa.europa.eu/en/nda/ndaclaims.htm

EFSA guidance on scientific requirements for specific types of claims

- which relationships are eligible for health claims
- what types of studies, outcome measures and study groups are appropriate:
  - Gut, immune
  - Bone, joints, skin, oral
  - Appetite, body weight, blood glucose
  - Antioxidants, cardiovascular
  - Physical performance
  - Neurological, psychological

http://www.efsa.europa.eu/en/nda/ndaclaims.htm

Conclusions

- the EU Commission has authorised 241 health claims to date based on assessment of substantiation by EFSA

- EFSA has defined scientific criteria for substantiation and has provided extensive guidance to applicants

- EFSA's work on assessment of health claims
  - has highlighted a number of key issues for substantiation which need to be considered by applicant
  - will help set future directions for research and will guide innovation