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
• 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?

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

Defining the claim
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:
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)

<table>
<thead>
<tr>
<th>Claim</th>
<th>Food/constituent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain development + eye development in foetus, infant</td>
<td>DHA (maternal)</td>
</tr>
<tr>
<td>Visual development in infant</td>
<td>DHA (infant)</td>
</tr>
<tr>
<td>Growth &amp; development of children</td>
<td>ALA, LA</td>
</tr>
<tr>
<td>Cognitive development</td>
<td>Iron</td>
</tr>
</tbody>
</table>
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)

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

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

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

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