



Guidance from EFSA opinions for study design and future applications

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Criteria peer-review

Prof. Albert Flynn (chair NDA-Panel):

“scientific criteria peer review and criteria for scientific evaluation HC applications are the same”

Only: the objective is different!

Outline

- Scientific criteria peer-review versus evaluation health claims substantiation
- (Isolated) soy protein and cholesterol - confusion!
- Skin photoprotection - generally accepted scientific concept?
- Immunity - mission impossible?
- Scientific criteria peer-review versus evaluation health claims substantiation - **Implications**

Objectives peer-review?

To establish:

- Significant advance in an experimental method, clinical practice, or fundamental scientific knowledge
- Originality and quality of research

Objectives EFSA evaluation?

To establish:

- Cause and effect relationship
- Food constituent defined and characterized
- Claimed effect physiologically beneficial



Grading Scientific Evidence

Grade of recommendation	Evidence level	Type of studies
A	1	1a Systematic review of randomised controlled trials (RCT) of good methodological quality and with <u>homogeneity</u> 1b Individual RCT with narrow confidence interval 1c Non-controlled studies
B	2	2a Systematic review of cohort studies (with homogeneity) 2b Individual cohort studies (including low quality RCT, eg <80% follow-up) 2c Non-controlled cohort studies/ecological studies
	3	3a Systematic review of case-control studies (with homogeneity) 3b Individual case-control studies
C	4	Case series/poor quality cohort or case-control studies
D	5	Expert opinion without explicit critical appraisal or based on physiology, bench research or "first principles"

(Isolated) soy protein

Food constituent

Meta-analyses may wrong-foot you!

Soy protein and lowering of LDL-cholesterol

Regular consumption of 1 to 2 servings of soy protein daily (15 to 30 g) has a significant favorable impact on serum lipoprotein risk factors for CHD.

Anderson & Bush. J Am Coll Nutr. 2011 Apr;30(2):79-91.

(Isolated) soy protein

Food constituent

EFSA opinion

(Isolated) Soy protein and lowering of LDL-cholesterol

Cause and effect relationship not established

EFSA J. 2010;8(7):1688

EFSA J. 2012;10(2):2555

Photoprotection

generally accepted scientific concept

J Nutr. 2011 Jun;141(6):1202-8. Epub 2011 Apr 27.

Green tea polyphenols provide photoprotection, increase microcirculation, and modulate skin properties of women.

Heinrich U, Moore CE, De Spirt S, Tronnier H, Stahl W.

Institute for Experimental Dermatology, University of Witten-Herdecke, D-58455 Witten, Germany.

Claim: photoprotection

Evidence: Significant reduction of UV-induced erythematous response

Judgement Peer-review: acceptable for publication ('cause-and-effect relationship established?')

Photoprotection

Concept according EFSA

Opinion beta-carotene related health claims

EFSA panel notes:

1. UV-induced erythema (sunburn or skin reddening) is a primary reaction of the skin following overexposure to UV (sun) light
2. it represents an inflammatory response of cutaneous tissue as a consequence of light-dependent molecular and cellular damage.

Photoprotection

Concept according EFSA

Opinion beta-carotene and photoprotection

EFSA panel **also** notes:

1. reduction in skin erythema (skin redness) after UV light or sun exposure **MAY** indicate a reduction in UV-induced skin damage
2. However, it can also reflect a reduction in the capacity of the skin to react to molecular and cellular damage

Photoprotection

Concept according EFSA

EFSA requires further proof that food constituent does not inhibit inflammatory reaction (reduction skin redness)!

Health claim on the function of the immune system

- Stimulation of immune parameters per se is not necessarily beneficial
- Changes in markers of inflammation per se do not necessarily indicate a beneficial physiological effect.

Health claim on the function of the immune system related to defence against pathogens

Acceptable marker of immune function (EFSA Guidance):

Stimulation of protective antibody titers, as measured by increased number of individuals attaining protective levels

Claim:

Defence against pathogens by stimulating immunologic responses

A measure that might be enough:

Stimulation of protective antibody response to vaccination

Protective antibody titres

Number of protected individuals

Prof. Henk van Loveren, KNAW 26 March 2012

Elderly!

- Seasonal trivalent inactivated Influenza Vaccination-model - protective antibody titers
- CD8+ T cells have been found to be essential for effective clearance and recovery from influenza infection (McMichael et al. NEJM, 1983)
- Correlates of clinical protection may not be measured using standard techniques such as antibody titers to predict vaccine efficiency (McElhaney et al. 2011)
- Influenza-specific memory CD8 T cells may be a predictive indicator of a vaccine responsive healthy immune system in old age. (Wagar et al., 2012)

Endothelium-dependent vasodilation

- Additional risk factor for cardiovascular events (in low-risk populations).
- Various methods to measure EDV
- Flow-mediated dilation (FMD) of the brachial artery (BA) widely accepted
- Large interlaboratory variation FMD BA measurements!

Walnuts & endothelium-dependent vasodilation

- One pertinent study in healthy human hypercholesterolemic volunteers (Ros et al., 2004)
- One supportive study in medicated type 2 diabetes patients (Ma et al., 2010)
- One supportive acute study (Cortès et al., 2006)

Acceptable for art. 13.5/14 claim?

Peer-review & EFSA

Many peer-reviewed studies declined by EFSA

Many scientist said to agree with EFSA's judgement!

Proprietary paper declined by EFSA accepted by peer-review

(Gleeson et al. Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *Int J Sport Nutr Exerc Metab.* 2011 Feb;21(1):55-64.)

Apparently, peer-reviewers do not agree with EFSA's judgement!

Peer-review & EFSA

Indeed,
scientific criteria acceptance peer-reviewed journal
apparently differ from
scientific criteria for health claim substantiation!

Implications

Published, 'old' studies should be meticulously screened for potential flaws in study methodology/statistics before paper can be included as pertinent

Newly designed studies should be targeted at HC substantiation - 'proof' vs. 'significant advance'

- 'Established' methodologies
- 'Validated' techniques

Beware!

- Be mindful of the 'peer-review mindset' when collaborating with CRO/academic group



A vibrant landscape featuring a large field of colorful tulips in various shades of red, orange, yellow, pink, and purple, arranged in neat rows. In the background, a traditional Dutch windmill stands prominently against a bright blue sky filled with large, fluffy white clouds. The scene is set in a lush green field with some trees and a small building visible in the distance.

Thank you!

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