



EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) ; Guidance on the scientific requirements for health claims related to bone, joints, skin and oral health

EFSA Publication

Link to article, DOI:
[10.2903/j.efsa.2012.2702](https://doi.org/10.2903/j.efsa.2012.2702)

Publication date:
2012

Document Version
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):
EFSA Publication (2012). *EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) ; Guidance on the scientific requirements for health claims related to bone, joints, skin and oral health*. European Food Safety Authority. EFSA Journal Vol. 10 No. 5 <https://doi.org/10.2903/j.efsa.2012.2702>

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SCIENTIFIC OPINION

Guidance on the scientific requirements for health claims related to bone, joints, skin, and oral health¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

The Panel on Dietetic Products, Nutrition and Allergies (NDA) has been asked by the European Food Safety Authority (EFSA) to draft guidance on the scientific requirements for health claims related to bone, joints, skin, and oral health. This guidance has been drawn from scientific opinions of the NDA Panel on such health claims. Thus, this guidance document represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. It is not intended that the document should include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. A draft of this guidance document, endorsed by the NDA Panel on 25 March 2011, was released for public consultation from 26 April 2011 to 31 August 2011.

KEY WORDS

Health claims, scientific requirements, bone, joints, skin, oral health.

¹ On request from EFSA, Question No EFSA-Q-2010-01184, adopted on 25 April 2012.

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³ Acknowledgement: The Panel wishes to thank for the preparatory work on this scientific opinion the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Bone/Teeth/Connective Tissue: Rikke Andersen, Olivier Bruyère, Albert Flynn, Ingegerd Johansson, Jukka Meurman and Hildegard Przyrembel.

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BACKGROUND AS PROVIDED BY EFSA

Regulation (EC) No 1924/2006⁴ harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. According to the Regulation, health claims should only be authorised for use in the Community after a scientific assessment of the highest possible standard has been carried out by EFSA.

EFSA and its NDA Panel have been engaging in consultation with stakeholders and have published guidance on the scientific substantiation of health claims since 2007⁵. Most recently, a briefing document on the scientific evaluation of health claims was published for consultation in April 2010, followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010⁶.

Based on experiences gained with the evaluation of health claims, and to further assist applicants in preparing and submitting their applications for the authorisation of health claims, the NDA Panel is asked to develop guidance documents on the scientific requirements for the substantiation of health claims in selected areas, in addition to the guidance for the scientific substantiation of health claims related to gut and immune function (EFSA-Q-2010-01139).

TERMS OF REFERENCE AS PROVIDED BY EFSA

The NDA Panel is requested by EFSA to develop guidance documents on the scientific requirements for health claims in the following areas:

- Post-prandial blood glucose responses/blood glucose control
- Weight management, energy intake and satiety
- Protection against oxidative damage
- Cardiovascular health
- Bone, joints, and oral health
- Neurological and psychological functions
- Physical performance

Specific issues to be addressed in these guidance documents include:

- which claimed effects are considered to be beneficial physiological effects?
- which studies/outcome measures are appropriate for the substantiation of function claims and disease risk reduction claims?

Each guidance document should be subject to public consultation, and may be followed up as appropriate by scientific meetings with experts in the field.

Before the adoption of each guidance document by the NDA Panel the draft guidance shall be revised, taking into account the comments received during the public consultation. A report on the outcome of the public consultation for each guidance document shall be published. All guidance documents should be finalised by July 2012.

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

⁵ <http://www.efsa.europa.eu/en/nda/ndaclaims.htm>

⁶ <http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf>

ASSESSMENT

1. Introduction

To assist applicants in preparing and submitting their applications for the authorisation of health claims, EFSA and in particular its Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) has ongoing consultations with stakeholders, and has published guidance on the scientific substantiation of health claims since 2007⁷. In April 2010, a draft briefing document on the scientific evaluation of health claims was published for consultation and was followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010. The draft briefing document has been transformed into a Panel output, taking into account the questions/comments received. This document constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims, and outlines the approach of the NDA Panel to the evaluation of health claims in general. In response to requests from industry, EFSA is engaged in further consultation with stakeholders, and is developing additional guidance on specific types of claims.

The present guidance, prepared by the NDA Panel, on the scientific requirements for the substantiation of health claims related to bone, joints, skin, and oral health was, prior to its finalisation, endorsed by the NDA Panel on 25 March 2011 for public consultation, which was open from 26 April to 31 August 2011. All the public comments received that related to the remit of EFSA were assessed, and the guidance has been revised taking into consideration relevant comments. The comments received and a report on the outcome of the public consultation have been published on the EFSA website.

The guidance document focuses on two key issues regarding the substantiation of health claims related to bone, joints, skin, and oral health:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

Issues which are related to substantiation and are common to health claims in general (e.g. characterisation of the food/constituent) are addressed in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims⁸.

This document has been drawn from scientific opinions of the NDA Panel on health claims related to bone, joints, skin, and oral health. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. The document should be read in conjunction with the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

It is not intended that the document should include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. Given that health claims are often technically complex and unique, additional health relationships and outcome measures for claimed

⁷ <http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm>

⁸ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

effects need to be considered in the context of a specific application. This guidance document may be updated in the future in light of additional experience gained with the evaluation of health claims.

2. General considerations

2.1. Beneficial physiological effects

According to Regulation (EC) No 1924/2006, the use of health claims shall only be permitted if the food/constituent, for which the claim is made, has been shown to have a beneficial physiological effect. In assessing each claim, the NDA Panel makes a scientific judgement on whether the claimed effect is considered to be a beneficial physiological effect in the context of the specific claim, as described in the information provided and taking into account the population group for whom the claim is intended. For function claims, a beneficial effect may relate to maintenance or improvement of a function.

For reduction of disease risk claims, 'beneficial' refers to whether the claimed effect relates to the reduction (or beneficial alteration) of a risk factor for the development (onset) of a human disease (not to the reduction of the risk of disease). A risk factor is a factor associated with the risk of a disease that may serve as a predictor of development of that disease. Whether or not the alteration of a factor is considered to be beneficial in the context of a reduction of disease risk claim depends on the extent to which it is established that:

- The factor is an independent predictor of disease risk (such a predictor may be established from intervention and/or observational studies);
- The relationship of the factor to the development of the disease is biologically plausible.

Except for well established risk factors, the extent to which the reduction of a factor is beneficial in the context of a reduction of disease risk claim needs to be considered on a case-by-case basis.

The NDA Panel considers that the population group for which health claims are intended is the general (healthy) population or specific subgroups thereof, for example, elderly people, physically active subjects, or pregnant women. In its evaluation, the NDA Panel considers that where a health claim relates to a function/effect which may be associated with a disease, subjects with the disease are not the target population for the claim, for example, joint health and osteoarthritis patients. Applications for claims which specify target groups other than the general (healthy) population are the subject of ongoing discussions with the Commission and Member States with regard to their admissibility.

The NDA Panel also considers whether the claimed effect is sufficiently defined to establish that the studies identified for substantiation of the claim were performed with (an) appropriate outcome measure(s) of that claimed effect. Reference to general, non-specific benefits of the nutrient or food for overall good health or health-related well-being may only be made if accompanied by a specific health claim.

2.2. Studies/outcome measures appropriate for substantiation of claims

As human studies are central for substantiation of health claims, this document focuses in particular on such studies. In considering whether the studies provided are pertinent (i.e. studies from which conclusions can be drawn for the scientific substantiation of the claim), the NDA Panel addresses a number of questions, including:

- Whether the studies have been carried out with the food/constituent for which the claim is made. This requirement means that there should be sufficient definition of the food/constituent for which the claim is made, and of the food/constituent that has been investigated in the studies which have been provided for substantiation of the claim. The evaluation also considers how the conditions under which the human studies were performed relate to the conditions of use (e.g. quantity and pattern of consumption of the food/constituent) proposed for the claim.
- Whether the design and quality of the studies allow conclusions to be drawn for the scientific substantiation of the claim. The evaluation takes into account the hierarchy of evidence as described in the scientific and technical guidance of the NDA Panel⁹, for example, intervention studies generally provide stronger evidence than observational studies. Intervention studies should be appropriately conducted so as to minimise bias. In observational studies, adequate control for factors other than the food/constituent which are known to have an impact on the claimed effect is important. Each health claim is assessed separately and there is no pre-established formula as to how many or what type of studies are needed to substantiate a claim. In this regard, the reproducibility of the effect of the food/constituent as indicated by consistency between studies is an important consideration.
- Whether the studies have been carried out in a study group representative of the population group for which the claim is intended. Can the results obtained in the studied population be extrapolated to the target population? For studies in groups (e.g. subjects with a disease) other than the target group for a claim (e.g. the general population), the NDA Panel considers on a case-by-case basis the extent to which it is established that extrapolation from the study group to the target group is biologically plausible.
- Whether the studies used (an) appropriate outcome measure(s) of the claimed effect. For this, the NDA Panel considers what is generally accepted in the relevant research fields (e.g. guidelines published by scientific societies based on rigorous methodological approaches), and consults experts from various disciplines, as appropriate.

3. Bone

3.1. Function claims

Contribution to the development and maintenance of normal bone throughout the lifespan is considered to be a beneficial physiological effect. Evidence for the scientific substantiation of these claims can be obtained from human studies by assessing the relationship between the food/constituent and measures of bone mass and bone mineral density (BMD) using appropriate methods of measurement (e.g. dual-emission X-ray absorptiometry (DXA)) and study duration (e.g. at least one year). Biochemical markers of bone turnover (of bone formation and resorption) can be used as supportive evidence/evidence for a mechanism by which the food/constituent could exert the claimed effect. An increase in bone formation and/or a decrease in bone resorption are considered beneficial physiological effects when they lead to an increase (or reduced loss) in BMD. For health claims on bone development (i.e. related to population subgroups prior to the achievement of peak bone mass, such as infants, children, adolescents and young adults), bone mineral content (BMC) may also be used as an appropriate outcome measure if adequately adjusted for changes in body mass/bone size.

⁹ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1). EFSA Journal,9(5):2170, 36 pp.

3.2. Disease risk reduction claims

For reduction of disease risk claims in older adults, falling is considered as a risk factor for osteoporotic fractures and reduction of the risk of falling, therefore, is a beneficial physiological effect by reducing the risk for osteoporotic fractures. The risk of falls and the risk of falling at least once are appropriate outcome measures for the assessment of the risk of falling in human intervention studies. The risk of falls and the risk of falling at least once are appropriate outcome measures for the assessment of the risk of falling in human intervention studies.

While it is generally accepted that reduced BMD is associated with an increased risk of osteoporotic fractures, increases in BMD (by dietary modification or drugs) have not generally been shown to reduce the risk of osteoporotic fractures in humans. For example, increasing BMD, or limiting the reduction of BMD in older adults, including post-menopausal women, has been shown to reduce the risk of osteoporotic fractures following certain dietary interventions (e.g. calcium supplementation) but not others (e.g. fluoride supplementation). Therefore, reduced BMD may be considered as a risk factor for osteoporotic fractures if an increase in (or reduced loss of) BMD following a particular nutritional intervention is accompanied by evidence of reduced bone fracture incidence in humans. There is also evidence for an association of bone turnover rate and risk of bone fractures. Markers of bone turnover may be considered as risk factors for osteoporotic fractures only if changes in these markers are accompanied by evidence of reduced bone fracture incidence in humans.

3.3. Study populations

Results from studies conducted in adult subjects with osteopenia/osteoporosis treated with lifestyle measures only could be used for the scientific substantiation of claims on the maintenance of bone, and of disease risk reduction claims. For studies in subjects with osteopenia/osteoporosis under pharmacological treatment for the prevention of osteoporotic fractures (e.g. bisphosphonates, selective oestrogen receptor modulators), the rationale for extrapolation of the results to the target population for the claim should be provided and will be considered on a case-by-case basis (e.g. evidence for a lack of interaction between the food/constituent and the medications used on the claimed effect).

4. Joints

4.1. Function claims

Claims related to muscle strength have already been addressed in the Guidance on the scientific requirements for health claims related to physical performance¹⁰.

Maintenance (i.e. reduced loss) of joint function can be considered a beneficial physiological effect. Possible outcomes related to joint function include mobility, stiffness and (dis)comfort (e.g. pain). Outcome measures which may be appropriate for the assessment of the claimed effect in humans should be indicated. For example, validated protocols and procedures under well-defined testing conditions using appropriate goniometers have been used to assess the mobility of different joints (e.g. knee, ankle); validated questionnaires could be used for the assessment of joint stiffness and (dis)comfort. For self-reported outcome measures, adequate blinding of subjects is particularly important.

Also changes in joint structure (e.g. changes in joint space width or other relevant measurements) leading to maintenance (i.e. reduced loss) of joint function(s) can be considered beneficial physiological effects. Evidence on whether (and the extent to which) specific changes in joint

¹⁰ <http://www.efsa.europa.eu/en/ndaclaims/ndaguidelines.htm>

structure may lead to changes in joint function should be provided and will be considered on a case-by-case basis. Structural changes in joint tissues, or changes in biochemical markers of, for example, collagen turnover, cartilage regeneration or joint inflammation (among others), that are proposed as mechanisms by which the food/constituent may exert the claimed effect on joint function will be considered on a case-by-case basis.

4.2. Disease risk reduction claims

An increased rate of joint cartilage degeneration may be considered a risk factor for the development (onset) of osteoarthritis (degenerative arthrosis). Studies measuring net cartilage loss (e.g. changes in joint space width or other relevant measurements) could be used for the scientific substantiation of disease risk reduction claims related to osteoarthritis.

Changes in markers of cartilage degeneration or of collagen turnover have not generally been shown to reduce the risk of osteoarthritis in humans and therefore are not considered acceptable as risk factors for disease risk reduction claims related to osteoarthritis.

4.3. Study populations

Results from studies performed in non-diseased (including high risk) population subgroups (e.g. Kell-Lawrence radiographic scores 0 or 1, obesity, knee varus or valgus malalignment) could be used for the scientific substantiation of health claims on joint function. Information on the selection and characterisation of the study population in relation to the claimed effect and a rationale for extrapolation of the results to the target population for which the claim is made should be provided and will be considered on a case-by-case basis.

The available scientific evidence does not establish that results obtained in patients with osteoarthritis (degenerative arthrosis) relating to the treatment of symptoms of this disease (e.g. erosion of articular cartilage, reduced mobility of joints) can be extrapolated to the target population for the claim (subjects without the disease). This is because normal cells and tissues are genetically (gene expression) and functionally different from osteoarthritic cells and tissues and therefore may respond differently to interventions with exogenous substances. In addition, the mechanisms involved in the onset and/or progression of osteoarthritis are largely unknown, so that it cannot be established that an intervention which has an effect on the progression of the disease (in patients with osteoarthritis), would also have an effect on its onset (subjects without the disease).

Studies on subjects with arthritis of various origins (rheumatoid arthritis, psoriatic arthritis, arthritis of infectious origin) and which relate to the treatment of symptoms of the disease cannot be considered for the scientific substantiation of health claims on joint function in the general population.

5. Teeth and gums

5.1. Function claims

Claims that refer to dental health, oral health, tooth protection and “teeth friendly” are too general for a scientific evaluation, and therefore need to be accompanied by a specific claim (e.g. claims addressed in Sections 5.1.1 to 5.1.5 of this guidance).

Contribution to the normal development of teeth is considered to be a beneficial physiological effect. For health claims on teeth development (i.e. related to population subgroups prior to the achievement of fully developed permanent teeth), outcome measures which may be appropriate for the assessment of the claimed effect in humans should be indicated.

5.1.1. Gums

Changes in gum structure leading to maintenance (i.e. reduced loss) of gum function(s) can be considered beneficial physiological effects. Evidence on whether (and the extent to which) specific changes in gum structure may lead to changes in gum function should be provided and will be considered on a case-by-case basis. For example, changes in the gingival index may lead to impaired protection of the teeth roots, which may remain exposed, for example, to the formation of dental plaque. Improving gum structure (e.g. the gingival index) is, therefore, considered a beneficial physiological effect. Gum structural changes which are proposed as mechanisms by which the food/constituent may exert the claimed effect on gum function will be considered on a case-by-case basis.

5.1.2. Plaque acid neutralisation and reduction of acid production in dental plaque

Plaque formation is a stepwise building of a bacterial biofilm on teeth and soft tissues, i.e. a highly specific initial attachment of bacteria to host receptors (e.g. cells), followed by secondary attachment of bacteria, binding to already colonising bacteria. Acid is produced in plaque through the fermentation of carbohydrates by acid-producing bacteria, and low plaque pH contributes to demineralisation of tooth tissues. Plaque acid neutralisation or the reduction of acid production in dental plaque may prevent demineralisation, and promote remineralisation of hydroxyapatite crystals, and are therefore considered beneficial physiological effects. Plaque acid/pH should be measured *in vivo* or *in situ* using appropriate methods. If tooth materials other than the human teeth are used *in situ* (e.g. animal tooth, synthetic tooth), evidence or a rationale for extrapolation of the results obtained in such tooth materials to human teeth (e.g. evidence on the degree of similarity to human teeth) should be provided and will be considered, on a case-by-case basis. *Ex vivo* studies are generally not appropriate because they do not reflect normal eating conditions but such studies can be used as evidence for a mechanism by which the food/constituent could exert the claimed effect.

5.1.3. Reduction of dental plaque and calculus

Dental plaque and calculus formation can contribute to adverse effects on dental health (e.g. in relation to approximal caries, gingivitis and periodontitis) when they occur at sites such as the cervical third, and interdentally below the approximal contact point between teeth, along the gingival margin, and in the fissures and pits of the teeth. A reduction in the amount of dental plaque and/or calculus at relevant sites may be a beneficial physiological effect. The amount of plaque or calculus can be measured *in vivo* and *in situ* using appropriate methods. If tooth materials other than human teeth are used *in situ* (e.g. animal tooth, synthetic tooth), evidence or a rationale for extrapolation of the results obtained in such tooth materials to human teeth (e.g. evidence on the degree of similarity to human teeth) should be provided and will be considered on a case-by-case basis. *Ex vivo* studies are generally not appropriate because they do not reflect normal eating conditions, but can be used as evidence for a mechanism by which the food/constituent could exert the claimed effect.

5.1.4. Maintenance of tooth mineralisation

Claimed effects referring to the promotion of tooth (re)mineralisation and/or the prevention of tooth demineralisation are interpreted as referring to a beneficial balance between de- and remineralisation of tooth enamel and dentin. Maintaining tooth mineralisation is considered a beneficial physiological effect.

Studies on tooth mineralisation including *in vivo* studies with dental caries and/or dental erosion as outcomes and *in situ* models can be used for the substantiation of these claims. If tooth materials other than human teeth are used *in situ* (e.g. animal tooth, synthetic tooth), evidence or a rationale for extrapolation of the results obtained in such tooth materials to human teeth (e.g. evidence on the

degree of similarity to human teeth) should be provided and will be considered on a case-by-case basis. *Ex vivo* studies are generally not appropriate because they do not reflect normal eating conditions, but such studies can be used as evidence for a mechanism by which the food/constituent could exert the claimed effect.

Claims for a beneficial effect of a food constituent (e.g. non/low-fermentable carbohydrates, intense sweeteners, and sugar alcohols) when used in replacement of a food constituent (e.g. sugars) with an independent role in increasing tooth demineralisation (e.g. by decreasing plaque pH) have been submitted. Substantiation may be based on evidence for an independent role of the replaced food constituent in increasing tooth demineralisation, together with evidence for the lack of an effect, or a reduced effect, of the food constituent which is used as a replacement.

5.1.5. Reduction of oral dryness

A dry mouth (i.e. symptoms because of a lowered saliva secretion or inadequate moistening/lubrication of oral tissues) may lead to oral discomfort, and to difficulties in swallowing and speaking. Therefore, reducing oral dryness is considered a beneficial physiological effect. Changes in oral dryness can be assessed *in vivo* by measuring saliva flow or by measuring self-perceived oral dryness using validated questionnaires.

Regarding the study groups for claims on oral dryness, it will be considered on a case-by-case basis whether the study group is representative of the target population for the claim (which cannot be a diseased population) with respect to the status of the salivary glands and ducts. Evidence should be provided that the mechanism by which the food/constituent exerts the claimed effect in the study group could be relevant for the target group for which the claim is made.

5.2. Disease risk reduction claims

There is evidence, for example, that colonisation by *Streptococcus mutans*, and the amount of dental plaque in particular locations are associated with an increased risk of gingivitis and dental caries. Also a decrease in plaque pH is associated with an increased risk of dental caries. A reduction of colonisation by *Streptococcus mutans*, a reduction of dental plaque in particular locations, and an increase in plaque pH have been associated with reduction in the incidence of dental caries following certain dietary interventions (e.g. frequent consumption of xylitol-sweetened and other sugar-free chewing gums). However, isolated changes in any of these factors have not generally been shown to reduce the risk of gingivitis or dental caries. Therefore, these factors may be considered as risk factors for gingivitis and/or dental caries only if changes in these factors are accompanied by evidence of reduced incidence of these diseases in humans in the context of a particular nutritional intervention.

6. Connective tissue

6.1. Claims on collagen formation

Collagen is a structural component of many tissues in the body including bones, cartilage, gums, skin, tendons and blood vessels. Contribution to normal collagen formation is therefore considered a beneficial physiological effect. Claims on contribution to normal collagen formation have been submitted for essential micronutrients (e.g. vitamin C). The scientific substantiation of these claims was based on the established biochemical role of such nutrients in collagen synthesis.

Increasing net collagen formation, or reducing net collagen breakdown, leading to maintenance (i.e. reduced loss) of tissue function(s) (e.g. bones, cartilage, gums, skin, tendons and blood vessels) can be considered beneficial physiological effects. Evidence on whether (and the extent to which)

specific changes in net collagen formation or breakdown may lead to changes in tissue function should be provided, and will be considered on a case-by-case basis. Structural changes in tissues or changes in biochemical markers of, for example, collagen turnover (among others) that are proposed as mechanisms by which the food/constituent may exert the claimed effect on tissue function will be considered on a case-by-case basis.

6.2. Claims on maintenance of skin function

Changes in skin structure contributing to the maintenance (i.e. reduced loss) of skin function can be considered beneficial physiological effects. Evidence on whether (and the extent to which) specific changes in skin structure may lead to changes in skin function should be provided, and will be considered on a case-by-case basis.

Maintenance (i.e. reduced loss) of the barrier functions of the skin is considered a beneficial physiological effect. The barrier functions of the skin include the permeability barrier (limiting water loss), the antioxidant barrier (protecting cells and molecules against oxidative damage), the photo-protection barrier (protecting cells and molecules against UV-induced damage), and the immune barrier (protection against pathogens).

Health claims on the maintenance of normal structure, hydration, elasticity or appearance of the skin do not necessarily refer to a particular physiological function of the skin as required by Regulation (EC) No 1924/2006. Also a decrease in wrinkles, which may be related to the maintenance or improvement of skin structure/hydration/elasticity, does not necessarily refer to a particular physiological function of the skin as required by Regulation (EC) No 1924/2006.

6.2.1. Claims on protection of the skin against dehydration

An impaired permeability barrier function of the skin leads to water loss from the *stratum corneum* and to skin dehydration. The associated symptoms include roughness of the skin with visible scaling and flaking, itching, and reduced resistance to shearing forces. Maintenance (i.e. reduced loss) of the permeability barrier function of the skin protects the skin against dehydration and is considered to be a beneficial physiological effect.

The scientific evidence for the substantiation of health claims on protection of the skin against dehydration can be obtained from human intervention studies showing a reduction in transepidermal water loss (TEWL) in normal conditions or after exposure to an irritant (e.g. sodium lauryl sulphate) using validated methods. Measures of the water-holding capacity of the *stratum corneum* of the skin or changes in signs/symptoms associated with skin dehydration may be used as supportive evidence. Structural changes in the skin (e.g. lipid content of the *stratum corneum*) may be proposed as mechanisms by which the food/constituent may exert the claimed effect.

6.2.2. Claims on protection of the skin against oxidative (including UV-induced) damage

Protection of the skin (cells and molecules such as DNA, proteins and lipids) from oxidative damage, including photo-oxidative (UV-induced) damage, may be a beneficial physiological effect because any significant oxidative modification of the target molecule may lead to a change in function. In this specific context, direct measurement of oxidative damage to skin with appropriate methods is required for substantiation. Guidance for the scientific substantiation of health claims related to protection of

body cells and molecules from oxidative (including photo-oxidative) damage has already been provided¹¹.

6.2.3. Claims on protection of the skin from UV-induced (other than oxidative) damage

Exposure to UV (sun) radiation may lead to DNA damage (e.g. pyrimidine dimers, strand breaks, and type I cell death (apoptosis)). Usually, the majority of DNA damage is repaired. However, incomplete or deficient repair may lead to skin lesions in the longer term (e.g. neoplasms). Therefore, decreasing DNA damage after UV radiation exposure is considered a beneficial physiological effect, which can be measured directly in skin biopsies.

Overexposure to UV (sun) radiation may also lead to depletion of Langerhans cells, which reflects direct damage to the immunological function of the skin. Therefore, decreasing depletion of Langerhans cells after UV light exposure is considered a beneficial physiological effect, which can be measured directly in skin biopsies.

Erythema (sunburn or skin reddening) is an inflammatory response of the skin to UV-induced molecular and cellular damage. If severe, sunburn may lead to blisters and loss of the barrier function of the skin. A reduction in UV-induced erythema (e.g. measured as change in minimal erythmal dose (MED) or erythema grade (reddening)) may indicate less UV-induced damage to the skin, but it can also reflect a reduction in the capacity of the skin to react to molecular and cellular damage. Therefore, UV-induced erythema cannot be used alone as an outcome measure for the substantiation of health claims on protection of the skin from UV-induced damage.

Delayed-type hypersensitivity (DTH) immune responses to recall antigens in the skin reflect a systemic effect of UV-radiation on the immune system, and cannot be considered in isolation as a marker of UV-induced damage to the skin. Therefore, DTH immune responses to recall antigens in the skin cannot be used alone as an outcome measure for the substantiation of health claims on protection of the skin from UV-induced damage.

CONCLUSIONS

The guidance document focuses on two key issues regarding the substantiation of health claims related to bone, joints, skin, and oral health:

- claimed effects which are considered to be beneficial physiological effects.
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

The document has been drawn from scientific opinions of the NDA Panel on health claims related to bone, joints, skin, and oral health. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas.

¹¹ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. Guidance on the scientific requirements for health claims related to antioxidants, oxidative damage and cardiovascular health. EFSA Journal, 9(12):2474, 13 pp.

GLOSSARY AND ABBREVIATIONS

BMC	Bone mineral content
BMD	Bone mineral density
DNA	Deoxyribonucleic acid
DTH	Delayed-type hypersensitivity
DXA	Dual-emission X-ray absorptiometry
MED	Minimal erythematous dose
UV	Ultraviolet
TEWL	Transepidermal water loss