European Food Safety Authority

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to vitamin D and normal function of the immune system and inflammatory response (ID 154, 159), maintenance of normal muscle function (ID 155) and maintenance of normal cardiovascular function (ID 159) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to vitamin D and normal function of the immune system and inflammatory response, maintenance of normal muscle function and maintenance of normal cardiovascular function. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claims is vitamin D, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that vitamin D is sufficiently characterised.

The claimed effects are normal function of the immune system and inflammatory response, maintenance of normal muscle function and maintenance of normal cardiovascular function. The target population is assumed to be general population.

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1 On request from the European Commission, Question No EFSA-Q-2008-941, EFSA-Q-2008-942, EFSA-Q-2008-946, adopted on 21 December 2009.

2 Panel members: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Monika Neuhäuser-Berthold, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Daniel Tomé, Hendrik van Loveren and Hans Verhagen. Correspondence: nda@efsa.europa.eu

3 Acknowledgement: The Panel wishes to thank for the preparation of this 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 Gut/Immune: Maria Carmen Collado, Miguel Gueimonde, Daisy Jonkers, Martinus Løvik, Bevan Moseley, Maria Saarela, Seppo Salminen, Stephan Strobel, Hania Szajewska and Hendrik van Loveren.

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The Panel concludes that a cause and effect relationship has been established between the dietary intake of vitamin D and contribution to the normal function of the immune system and healthy inflammatory response, and maintenance of normal muscle function.

The Panel considers that, in order to bear the claims, a food should be at least a source of vitamin D as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of vitamin D and maintenance of normal cardiovascular function.

KEY WORDS

Vitamin D, immune system, inflammatory response, muscle function, cardiovascular function, health claims.

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[4] submitted by Member States contains main entry claims with corresponding conditions of use and literature from similar health claims. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is vitamin D which is a well recognised nutrient and is measurable in foods by established methods. Vitamin D occurs naturally in foods as vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Different forms of vitamin D are authorised for addition to foods and for use in food supplements (Annex II of the Regulation (EC) No 1925/2006[5] and Annex II of Directive 2002/46/EC[6]). This evaluation applies to vitamin D naturally present in foods and those forms authorised for addition to foods and for use in food supplements (Annex II of the Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

The Panel considers that the food constituent, vitamin D, which is the subject of the health claim is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Normal function of the immune system and inflammatory response (ID 154, 159)

The claimed effect is "immune system" and "vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response". The Panel assumes that the target population is the general population.

The Panel considers that contribution to the normal function of the immune system and a healthy inflammatory response are beneficial physiological effects.

2.2. Maintenance of normal muscle function (ID 155)

The claimed effect is "muscle growth, development and function". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal muscle function is a beneficial physiological effect.

[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] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, p. 26–38.
[6] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51–57.

2.3. Maintenance of normal cardiovascular function (ID 159)

The claimed effect is "vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal cardiovascular function is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

Vitamin D can be obtained from dietary sources or can be synthesised in the body by exposure to UV-radiation from the sun. Even though it is more suitable to refer to vitamin D as a hormone, vitamin D resembles true vitamins, since humans deprived of solar exposure depend on a food source. Synthesis of vitamin D in the skin by the action of sunlight is insufficient to meet requirements in some European countries, especially during winter months when there is little sunlight exposure.

Vitamin D is biologically inactive and requires successive hydroxylations; first in the liver, where 25-hydroxyvitamin D (25-OHD) is formed, and the next hydroxylation in the kidneys form 1,25-dihydroxyvitamin D (1,25-$(OH)_2$D), which is the biologically active form of vitamin D. 1,25-(OH)2D interacts with a specific nuclear receptor in its target tissues that results in a biological response. The major target tissues for 1,25-$(OH)_2$D are the intestine and bone; however, nuclear receptors for 1,25-$(OH)_2$D have been identified in several other tissues and in cultured tumour cells. Serum concentration of 25-OHD is accepted as a valid marker of vitamin D status.

The principal physiological function of vitamin D in all vertebrates including humans is to maintain serum calcium and phosphorus concentrations in a range that supports cellular processes, neuromuscular function, and bone ossification. Vitamin D accomplishes this goal by enhancing the efficiency of the small intestine to absorb dietary calcium and phosphorous, and by mobilising calcium and phosphorus from the bone.

Vitamin D also has other functions in tissues not primarily related to mineral metabolism. One example is the haematopoietic system, in which vitamin D affects cell differentiation and proliferation including such effects also in cancer cells. Vitamin D furthermore participates in the process of insulin secretion. The active metabolite of vitamin D, 1,25$(OH)_2$D, regulate the transcription of a large number of genes through binding to a transcription factor, the vitamin D receptor (VDR) (SCF, 2002).

3.1. Normal function of the immune system and inflammatory response (ID 154, 159)

Vitamin D plays a regulatory role in the functioning of the immune system. A vitamin D receptor (VDR) was identified in peripheral mononuclear cells and in both T-helper 1 (Th1) and T-helper 2 (Th2) cells. 1,25$(OH)_2$D reduces the inflammatory response of Th1 cells, suppresses antigen presentation by dendritic cells, suppresses proliferation and immunoglobulin production and retards the differentiation of B cell precursors into plasma cells, exerting an inhibitory action on the adaptive immune system. 1,25$(OH)_2$D increases expression of cathelicidin (LL-37), an antimicrobial peptide thought to be important for the innate immune system, especially against *Mycobacterium tuberculosis* (Bikle, 2009; Cantorna et al., 2008; Khazai et al., 2008).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of vitamin D and contribution to the normal function of the immune system and healthy inflammatory response.

3.2. Maintenance of normal muscle function (ID 155)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus on the role of vitamin D in normal muscle function (Norman and Henry, 2007; Cotler et al., 2008).

Muscle weakness is a feature of the clinical syndrome of vitamin D deficiency. Clinical symptoms of vitamin D deficiency myopathy include proximal muscle weakness, diffuse muscle pain, and gait impairments such as waddling way of walking (Schott and Wills, 1976; Ceglia, 2008).

The vitamin D receptor is expressed in human muscle tissue, and its activation may promote *de novo* protein synthesis in muscle (Sorensen et al., 1979).

The Panel considers that a cause and effect relationship has been established between the dietary intake of vitamin D and maintenance of normal muscle function.

3.3. Maintenance of normal cardiovascular function (ID 159)

Ten references were provided to substantiate the claimed effect – three legislative texts (CEDAP,1997; NHPD 2009; ODAOIOUs, 1995), one guideline for the control of health claims (NFA, 2002), one consensus opinion (JHCI, 2003), one opinion from the authoritative body (SNF, 2004), three human studies (Armas et al., 2004; Patel at al., 2007; Shoji et al., 2004), and one *in vitro* study (Cohen-Lahav et al., 2007).

In the opinions from JHCI (2003) and SNF (2004) the relationship between dietary intake of vitamin D and function of circulatory system is not mentioned.

Shoji et al. (2004) evaluated the effect of vitamin D3 analogue supplementation on the risk of cardiovascular mortality in haemodialysis patients with end-stage renal disease. The Panel considers that in this study the effect of vitamin D analogue given for medical purposes was assessed and no evidence was provided that haemodialysis patients are representative of the target population with regard to vitamin D status.

The association between serum 25(OH)D level and chosen clinical and laboratory markers of disease activity in patients with early inflammatory polyarthritis was studied by Patel at al. (2007). Armas et al. (2004) compared the effect of the same single dose of vitamin D2 and D3 (50.000 IU taken orally) on serum 25(OH)D concentration. In an *in vitro* study, the mechanism of inhibition of $1,25(OH)_2D3$ and $1,24(OH)_2D2$ on TNFα expression in macrophages was investigated (Cohen-Lahav et al., 2007). The Panel notes that the endpoints studied did not relate to the claimed effect and therefore no conclusions can be drawn from these studies for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of vitamin D and maintenance of normal cardiovascular function.

4. Panel's comments on the proposed wording

4.1. Normal function of the immune system and inflammatory response (ID 154, 159)

The following wording reflects the scientific evidence: "Vitamin D contributes to the normal function of the immune system and healthy inflammatory response.".

4.2. Maintenance of normal muscle function (ID 155)

The following wording reflects the scientific evidence: "Vitamin D contributes to the maintenance of normal muscle function.".

5. Conditions and possible restrictions of use

The Panel considers that in order to bear the claim a food should be at least a source of vitamin D as per Annex to Regulation (EC) 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population. Tolerable Upper Intake Levels (UL) have been established as 50 µg/day for adults including pregnant and lactating women. For children (0 – 10 years) and adolescents (11 – 17 years) UL were established as 25µg/day and 50µg/day respectively (SCF, 2002).

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, vitamin D, which is the subject of the health claims is sufficiently characterised.

Normal function of the immune system and inflammatory response (ID 154, 159)

- The claimed effect is "immune system" and "vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response". The target population is assumed to be the general population. Contribution to the normal function of the immune system and a healthy inflammatory response are beneficial physiological effects.

- A cause and effect relationship has been established between the dietary intake of vitamin D and contribution to the normal function of the immune system and healthy inflammatory response.

- The following wording reflects the scientific evidence: "Vitamin D contributes to the normal function of the immune system and healthy inflammatory response.".

Maintenance of normal muscle function (ID 155)

- The claimed effect is "muscle growth, development and function". The target population is assumed to be the general population. Maintenance of normal muscle function is a beneficial physiological effect.

- A cause and effect relationship has been established between the dietary intake of vitamin D and maintenance of normal muscle function.

- The following wording reflects the scientific evidence: "Vitamin D contributes to the maintenance of normal muscle function.".

Maintenance of normal cardiovascular function (ID 159)

- The claimed effect is "Vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response". The target population is assumed to be the general population. Maintenance of normal cardiovascular function is a beneficial physiological effect.

- A cause and effect relationship has not been established between the dietary intake of vitamin D and maintenance of normal cardiovascular function.

Conditions and possible restrictions of use

In order to bear the claims a food should be at least a source of vitamin D as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13(1) of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-941, EFSA-Q-2008-942, EFSA-Q-2008-946). The scientific substantiation is based on the information provided by the Members States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/panels/nda/claims/article13.htm

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APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[7] (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

a) the role of a nutrient or other substance in growth, development and the functions of the body; or

b) psychological and behavioural functions; or

c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[8]

Foods are commonly involved in many different functions[9] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

[7] OJ L12, 18/01/2007
[8] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[9] The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

(a) the claimed effect of the food is beneficial for human health,

(b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.

- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.

- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.

- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.

- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.

- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to vitamin D, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
154	Vitamin D	Immune system	Vitamin D is important for the immune system/natural defences
	Conditions of use - 15-30 µg= 600-1200 I.E. - Must at least be a source of vitamin/s as per annex to Regulation 1924/2006 - Number of nutrients/other substances that are essential to claimed effect: 1. Names of nutrient/other substances and Quantity in Average daily serving: 5 microgram(s) Vitamin D. Daily amount to be consumed to produce claimed effect: 5 microgram(s). Length of time after consumption for claimed effect to become apparent: Regular consumption. Other conditions for use: comply with "source of" nutrition claim in 1924/2006/EC		
155	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
	Vitamin D	Muscle growth, development and function	Vitamin D helps build and maintain strong muscles Vitamin D is needed for proper functioning of the muscles Vitamin D helps maintain muscle function in ageing
	Conditions of use - Must at least be a source of vitamin/s as per annex to Regulation 1924/2006 - Number of nutrients/other substances that are essential to claimed effect: 1. Names of nutrient/other substances and Quantity in Average daily serving: 5 microgram(s) vitamin D. Daily amount to be consumed to produce claimed effect: 5 microgram(s). Length of time after consumption for claimed effect to become apparent: Regular use. Other conditions for use: comply with "source of" nutrition claim in 1924/2006/EC - 5 µg per day		
159	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
	Vitamin D3	Vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response	Vitamin D3 has long been known to aid in calcium absorption, but new research shows that D3 also plays a role in cardiovascular function and supports healthy inflammatory response Vitamin D3 has long been known to aid in calcium absorption, but new resea
	Conditions of use - 500-1000 mg Calcium als Calciumcitrat, 10 µg Vitamin D, 8-16 mg Zink - D3 Recommended Daily dosage 200-400iu. D3 Product Dosage 4.5µg: 100% RDA. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006.		

GLOSSARY / ABBREVIATIONS

VDR	Vitamin D receptor
Th1	T-helper 1
Th2	T-helper 2
TNFα	Tumor necrosis factor α