



EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to lutein and maintenance of normal vision (ID 1603, 1604, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

EFSA Publication

Link to article, DOI:
[10.2903/j.efsa.2012.2716](https://doi.org/10.2903/j.efsa.2012.2716)

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); Scientific Opinion on the substantiation of health claims related to lutein and maintenance of normal vision (ID 1603, 1604, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006*. European Food Safety Authority. the EFSA Journal Vol. 10(6) No. 2716 <https://doi.org/10.2903/j.efsa.2012.2716>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to lutein and maintenance of normal vision (ID 1603, 1604, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

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 in the framework of further assessment related to lutein and maintenance of normal vision. The food constituent that is the subject of the claim, lutein, is sufficiently characterised. The claimed effect, maintenance of normal vision, is a beneficial physiological effect. The proposed target population is the general population. In weighing the evidence, the Panel took into account that one human intervention study in healthy subjects did not show an effect of lutein on visual acuity or glare sensitivity, that the results of this study were inconsistent as regards contrast sensitivity, and that the evidence provided for a mechanism by which lutein could exert the claimed effect in vivo in humans is weak. On the basis of the data presented, the Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of lutein and maintenance of normal vision.

© European Food Safety Authority, 2012

KEY WORDS

Lutein, vision, health claims.

¹ On request from the European Commission, Question No EFSA-Q-2012-00162 and EFSA-Q-2012-00163, adopted on 26 April 2012.

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 the members of the Working Group on Claims for the preparatory work on this scientific opinion: 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.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to lutein and maintenance of normal vision (ID 1603, 1604, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2012;10(6):2716. [17 pp.]. doi:10.2903/j.efsa.2012.2716. Available online: www.efsa.europa.eu/efsajournal

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. The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. This opinion addresses the scientific substantiation of a health claim in relation to lutein and maintenance of normal vision. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims, references that EFSA has received from Member States or directly from stakeholders and the additional information provided by the competent Authority of Austria for further assessment of this claim.

The food constituent that is the subject of the health claim is lutein. The Panel considers that lutein is sufficiently characterised.

The claimed effect, which is eligible for further assessment, is maintenance of normal vision. The proposed target population is the general population. Visual function, including visual acuity and contrast sensitivity, can be assessed by established methods. The Panel considers that maintenance of normal vision is a beneficial physiological effect.

The NDA Panel has already issued two opinions in relation to a claim on lutein and maintenance of normal vision, in which over 200 references which were considered. In the framework of further assessment three human intervention studies, of which only two were on healthy subjects, one human observational study and one case report, as well as a number of animal, *in vitro* and *ex vivo* studies were provided. This evaluation is based on the scientific references provided in the present and in the previous submissions which addressed the effects of lutein on maintenance of vision and/or on the mechanisms by which lutein could exert the claimed effect in the target population.

Two publications submitted reported on outcomes related to visual performance in a subgroup of subjects participating in a larger study (LUXEA) which aimed to address the safety of zeaxanthin and lutein supplements, and the accumulation of these carotenoids in the eye. The Panel notes that the visual performance study was not randomised, that no information was provided on how subjects were selected from the LUXEA study, that the statistical methods used for data analysis are poorly described in the publications, and that no information is provided about the baseline characteristics of the subjects for the variables of interest, or about their comparability between groups. The Panel also notes that the final sample size analysed for visual performance outcomes is small, and that the study was likely to be underpowered for such outcomes. The Panel considers that no conclusions can be drawn from the study reported in these two publications for the scientific substantiation of the claim.

A third publication reported on a study on measures of visual function in subjects who had long-term computer display light exposure after consumption of placebo or lutein supplementation. The Panel considers that this study does not show an effect of lutein on visual acuity or glare sensitivity, and that the results are inconsistent as regards contrast sensitivity.

A number of human intervention studies conducted in healthy populations investigated the effects of lutein on macular pigment optical density. The Panel notes that macular pigment optical density is not a measurement of visual function or a surrogate marker for age-related macular degeneration (AMD). The Panel also notes that significant changes in macular pigment optical density may not be accompanied by changes in functional outcomes related to vision or AMD risk, and that the predictive value of changes in macular pigment optical density as an indicator of improved vision has not been established. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of a claim on vision.

Some human intervention studies in patients with cataracts, diabetic retinopathy, age-related maculopathy or macular degeneration (designated together as ARM), or inherited retinal degeneration (e.g. retinitis pigmentosa), were also provided. The Panel notes that the evidence provided does not establish that results obtained in these patient population subgroups with respect to functional outcomes related to vision can be extrapolated to the target population for the claim. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of the claim.

Some observational studies investigated the association between estimated dietary intakes of lutein and zeaxanthin combined, or between lutein concentrations in blood, adipose tissue or the retina as markers of lutein intake, and different outcomes (e.g. macular pigment optical density; eye-related diseases such as ARM, cataracts, or diabetic retinopathy). The Panel notes that the relationship between estimated dietary intakes of lutein alone and these outcomes was not addressed in the studies. The Panel also notes that blood concentrations of lutein reflect lutein intakes over a short period of time, and therefore may not be representative of long-term consumption, and that blood and tissue concentrations of lutein are poorly correlated with dietary lutein intakes. The Panel considers that no conclusions can be drawn from these observational studies for the scientific substantiation of the claim.

One cross-sectional study investigated the association between dietary intakes of lutein and the presence (or history) of cataracts. The Panel notes that it is unclear from the publication how subjects were selected for the study and whether the examination of the medical history for cataracts was performed prior to or after recruitment. The Panel also notes that no information is provided on the extent to which current lutein intakes (i.e. retrieved after diagnosis of cataracts) may relate to past lutein intakes (i.e. which may have contributed to the development of cataracts). The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

With respect to the mechanism by which lutein could exert the claimed effect, a number of *in vitro* and *ex vivo* studies were submitted, which investigated the antioxidant activity of carotenoids, including lutein. The Panel notes that lutein can act as a free radical scavenger *in vitro*. However, the Panel considers that the evidence provided in these *ex vivo* and *in vitro* studies does not establish that these models could predict the occurrence of an effect of lutein on the protection of cells or molecules (e.g. DNA, proteins and lipids) in the human eye from oxidative damage *in vivo*.

In an animal study, the effect of lutein intake on visual function after light exposure thickness of outer nuclear layer of the enucleated eyes, photoreceptor cell apoptosis and light-induced DNA damage was investigated. The Panel notes that no evidence was provided on how this high dose of lutein in animals relates to a dose in humans. The Panel considers that no conclusions can be drawn from this animal study with respect to the mechanisms by which lutein could exert the claimed effect.

In weighing the evidence, the Panel took into account that one human intervention study in healthy subjects did not show an effect of lutein on visual acuity or glare sensitivity, that the results of this study were inconsistent as regards contrast sensitivity, and that the evidence provided for a mechanism by which lutein could exert the claimed effect *in vivo* in humans is weak.

On the basis of the data presented, the Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of lutein and maintenance of normal vision.

TABLE OF CONTENTS

Abstract	1
Summary	2
Table of contents	4
Background as provided by the European Commission	5
Terms of reference as provided by the European Commission	5
EFSA Disclaimer.....	5
Introduction	6
Assessment	6
1. Characterisation of the food/constituent (ID 1603, 1604).....	6
2. Relevance of the claimed effect to human health (ID 1603, 1604)	6
3. Scientific substantiation of the claimed effect (ID 1603, 1604).....	6
Conclusions	10
Documentation provided to EFSA	10
References	10
Appendices	12
Glossary and Abbreviations	17

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

EFSA DISCLAIMER

See Appendix B

INTRODUCTION

The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. These claims include already assessed claims related to micro-organisms which the Panel considered to be not sufficiently characterised and claims for which the NDA Panel concluded that there was insufficient evidence to establish a cause and effect relationship between the consumption of the food and the claimed effect.

Following an opinion of the NDA Panel on a health claim pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ in which the Panel concluded that the evidence provided was insufficient to establish a cause and effect relationship between lutein and maintenance of normal vision (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2010), EFSA received additional information from the competent Authority of Austria for further assessment of this claim.

ASSESSMENT

1. Characterisation of the food/constituent (ID 1603, 1604)

The food constituent that is the subject of the health claim is lutein, which is a xanthophyll carotenoid naturally present in food, especially in green leafy vegetables such as spinach and kale. The group of xanthophyll carotenoids also includes zeaxanthin, β -cryptoxanthin, neoxanthin and violaxanthin, among others. Lutein can be measured by established methods.

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

2. Relevance of the claimed effect to human health (ID 1603, 1604)

The claimed effect, which is eligible for further assessment, is maintenance of normal vision. The proposed target population is the general population.

For ID 1604, a request was made to interpret the claimed effect as contribution to the protection of the retina and the lens from oxidative damage. The Panel notes that ID 1604 together with ID 1603 have been previously assessed as a claim on maintenance of normal vision, and this is the claim which is eligible for further assessment as agreed by the European Commission and Member States.

Visual function, including visual acuity and contrast sensitivity, can be assessed by established methods.

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

3. Scientific substantiation of the claimed effect (ID 1603, 1604)

The Panel has issued two opinions in relation to a claim on lutein and maintenance of normal vision. The first opinion (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2010) was based on over 200 references which were collectively submitted under IDs 1603, 1604 and 1931. The second opinion (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011) was based

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.

on the references submitted under IDs 1779 and 2080, which did not provide any additional scientific data for the scientific substantiation of the claim.

In the framework of further assessment, the additional information provided (i.e. not evaluated previously by the Panel) included three human intervention studies (Berson et al., 2010; Ma et al., 2009; Rodriguez-Carmona et al., 2006), of which only two were on healthy subjects (Ma et al., 2009; Rodriguez-Carmona et al., 2006), one human observational study and one case report, as well as a number of animal, *in vitro* and *ex vivo* studies.

This evaluation is based on the scientific references provided in the present and the previous submissions which addressed the effects of lutein on maintenance of vision and/or on the mechanisms by which lutein could exert the claimed effect in the target population.

In this context, the Panel considers that human intervention studies which addressed the effects of lutein on functional measures of vision in the target population (i.e. subjects with normal vision) are pertinent for the scientific substantiation of the claim (Kvansakul et al., 2006; Ma et al., 2009; Rodriguez-Carmona et al., 2006).

Two publications (Kvansakul et al., 2006; Rodriguez-Carmona et al., 2006) reported on outcomes related to visual performance in a subgroup of subjects participating in a larger study (LUXEA) which aimed to address the safety of zeaxanthin and lutein supplements, and the accumulation of these carotenoids in the eye (Schalch et al., 2007). The LUXEA study was a double-blind, placebo-controlled, two phase trial in which 92 healthy male subjects (18-40 years) were randomised (23 subjects per group) to receive either lutein (L, 10 mg/day), zeaxanthin (Z, 10 mg/day), lutein and zeaxanthin (L+Z, 10 mg/day of each), or placebo (P, unspecified) for six months (phase 1). Five subjects per group agreed to continue the intervention for an additional six-month period (phase 2) during which they received double daily doses of the single carotenoids (L and Z groups), the same dose of the combination (L+Z group), or the combination of carotenoids (P group, 10 mg of each carotenoid per day). An additional group of 10 subjects was recruited at the end of phase 1 to serve as placebo in phase 2 of the study. Scattered light and high mesopic contrast acuity thresholds (CAT) (Kvansakul et al., 2006), as well as colour vision (Rodriguez-Carmona et al., 2006), were measured at the end of phase 1 in 34 out of 73 subjects who completed phase 1 (in 6, 8, 9 and 11 subjects from groups L, Z, L+Z and P) and in four (Kvansakul et al., 2006) or six (Rodriguez-Carmona et al., 2006) out of the 10 subjects from the new placebo group. These measures were repeated at the end of phase 2 in the 18 subjects who agreed to continue with the intervention (five subjects in groups Z, L+Z and P receiving L+Z, three subjects in group L), and in four (Kvansakul et al., 2006) or six (Rodriguez-Carmona et al., 2006) from the new placebo group. Macular pigment optical density (MPOD) was also measured at the end of phase 2 in these subjects. Between and within group changes in scattered light and CAT between phases 1 and 2 were assessed, as well as the relationship between changes in these outcomes as well as colour vision and MPOD measurements. The Panel notes that the visual performance study was not randomised, that no information was provided on how subjects were selected from the LUXEA study, that the statistical methods used for data analysis are poorly described in the publications, and that no information is provided about the baseline characteristics of the subjects for the variables of interest, or about their comparability between groups. The Panel also notes that the final sample size analysed for visual performance outcomes (five subjects per group or less) is small, and that the study was likely to be underpowered for such outcomes. The Panel considers that no conclusions can be drawn from the study reported in these two publications for the scientific substantiation of the claim.

A third publication (Ma et al., 2009) reported on a randomised, double-blind, placebo-controlled study which compared measures of visual function in 37 healthy subjects (22-30 years) who had long-term computer display light exposure (average computer usage time >10 h/day during the previous 2 years), and who received either a placebo (maltodextrin, n=12) or lutein supplementation (6 or

12 mg/day; n=12 and 13 respectively) for 12 consecutive weeks. Uncorrected visual acuity and best-spectacle corrected visual acuity were measured with decimal charts in standardised lighting conditions, and contrast sensitivity and glare sensitivity were measured with a contrast glare tester using concentric ring-shaped visual targets equivalent to visual angles of 6.3, 4.0, 2.5, 1.6 and 0.7°. Results for all these outcomes were expressed in logarithm. Habitual diet was assessed using a food-frequency questionnaire and three-day weighed food record at baseline and at the final study visit. Differences at baseline between groups were tested with the χ^2 -test or ANOVA, intra-group comparisons before and after supplementation were assessed using paired t-tests, and inter-group comparisons after supplementation were assessed with ANOVA. No power calculation was reported. The three groups did not differ at baseline in lutein intakes or in visual parameters, except for lower contrast sensitivity at 4.0° in the lutein group receiving 12 mg/day compared to placebo (p=0.045). This study did not find a significant effect of lutein supplementation (6 or 12 mg/day) on measures of visual acuity compared with placebo. Compared to placebo, contrast sensitivity was significantly higher at 2.5° (p=0.003) in the group supplemented with 6 mg/day lutein, but not in the group supplemented with 12 mg/day. No significant differences in glare sensitivity were observed between lutein (either group) and placebo. The Panel considers that this study does not show an effect of lutein on visual acuity or glare sensitivity, and that the results are inconsistent as regards contrast sensitivity.

The remaining human intervention studies in healthy populations either used lutein in combination with other components (e.g. antioxidant vitamins and other carotenoids), or examined the relationship between blood concentrations of lutein and health outcomes following dietary manipulations. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of a claim on lutein, particularly considering that the relationship between lutein intake and blood concentrations of lutein was not described in these studies.

A number of human intervention studies conducted in healthy populations investigated the effects of lutein on MPOD. The Panel notes that MPOD is not a measurement of visual function or a surrogate marker for age-related macular degeneration (AMD). The Panel also notes that significant changes in MPOD may not be accompanied by changes in functional outcomes related to vision or AMD risk, and that the predictive value of changes in MPOD as an indicator of improved vision has not been established (Bernstein et al., 2010; Davies and Morland, 2004; FDA, 2005). The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of a claim on vision.

Human intervention studies in patients with cataracts, diabetic retinopathy, age-related maculopathy or macular degeneration (designated together as ARM), or inherited retinal degeneration (e.g. retinitis pigmentosa), were also provided. The Panel notes that the majority of these studies used lutein in combination with other components (e.g. antioxidant vitamins and other carotenoids) and/or did not assess any functional outcomes related to vision, but rather changes in MPOD, whereas only a few studies assessed visual function. The Panel also notes that the evidence provided does not establish that results obtained in these patient population subgroups with respect to functional outcomes related to vision can be extrapolated to the target population for the claim. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of the claim.

A number of the observational studies provided, addressed endpoints unrelated to vision (e.g. plasma antioxidant capacity). Other observational studies investigated the association between estimated dietary intakes of lutein and zeaxanthin combined, or between lutein concentrations in blood, adipose tissue or the retina as markers of lutein intake, and different outcomes (e.g. MPOD; eye-related diseases such as ARM, cataracts, or diabetic retinopathy). The Panel notes that the relationship between estimated dietary intakes of lutein alone and these outcomes was not addressed in the studies. The Panel also notes that blood concentrations of lutein reflect lutein intakes over a short period of time, and therefore may not be representative of long-term consumption, and that blood and tissue concentrations of lutein are poorly correlated with dietary lutein intakes (FDA, 2005). The Panel

considers that no conclusions can be drawn from these observational studies for the scientific substantiation of the claim.

One cross-sectional study investigated the association between dietary intakes of lutein and the presence (or history) of cataracts (Rodriguez-Rodriguez et al., 2006) in 183 institutionalised men and women aged 65 years and over. Dietary intakes of some vitamins and carotenoids, including lutein, were estimated using a seven-day weighed food record. After exclusion of subjects who died soon after the beginning of the study or had congenital cataracts, 177 subjects were included in the analyses, of which 91 had cataracts or history of cataracts (cases) and 86 had not (controls). It is unclear from the publication how subjects were selected for the study and whether the examination of the medical history for cataracts was performed prior to or after recruitment. The Panel also notes that no information is provided on the extent to which current lutein intakes (i.e. retrieved after diagnosis of cataracts) may relate to past lutein intakes (i.e. which may have contributed to the development of cataracts). The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

With respect to the mechanism by which lutein could exert the claimed effect, a number of human intervention studies, narrative reviews and text books were provided in relation to the bioavailability and metabolism of lutein, and in relation to its role as a structural component of the eye. The Panel notes that dietary lutein is bioavailable, and that it is one of the carotenoids found in the macula of the human eye. A number of *in vitro* and *ex vivo* studies investigated the antioxidant activity of carotenoids, including lutein. These included four studies on the effect of lutein in eye tissues subjected to oxidative stress (two in cultures of rat retinal cells, one in porcine retinal homogenates, and one in cultured human retinal cells) and one study which investigated light-induced singlet oxygen generation in post-mortem human macula and retinal pigment epithelium/choroid. The Panel notes that lutein can act as a free radical scavenger *in vitro*. However, the Panel considers that the evidence provided in these *ex vivo* and *in vitro* studies does not establish that these models could predict the occurrence of an effect of lutein on the protection of cells or molecules (e.g. DNA, proteins and lipids) in the human eye from oxidative damage *in vivo*.

Sasaki et al. (2011) investigated in mice, after light exposure, the effect of lutein intake on visual function assessed with electroretinograms, thickness of outer nuclear layer of the enucleated eyes, photoreceptor cell apoptosis and light-induced DNA damage. Two groups of mice received a standard chow and another group received for 10 days the same chow supplemented with 0.1 % lutein, providing a daily lutein intake estimated to be 170 mg/kg body weight, which is about 500 times the maximum dose used in human interventions. One group on the control diet, and the supplemented group, were dark-adapted for 12 hours, then exposed to a single light exposure with 5,000 lux of a white fluorescence lamp over three hours. The number of animals per group varied between five and eight according to the results reported. The Panel notes that no evidence was provided on how this high dose of lutein in animals relates to a dose in humans. The Panel considers that no conclusions can be drawn from this animal study with respect to the mechanisms by which lutein could exert the claimed effect.

The remaining animal, *in vitro* and *ex vivo* studies provided were either not designed to assess the effects of lutein *per se* on the proposed outcomes (e.g. addressed the effects of carotenoids other than lutein, the effects of lutein in combination with other carotenoids (e.g. zeaxanthin), or the effects of xanthophyll-depleted diets with or without lutein supplementation), assessed outcomes unrelated to vision (e.g. inflammation; and cell damage and/or oxidative stress in bone marrow, blood or liver), or provided insufficient information for a scientific evaluation (e.g. letters to the editor). The Panel considers that no conclusions can be drawn from these references with respect to the mechanisms by which lutein could exert the claimed effect.

In weighing the evidence, the Panel took into account that one human intervention study in healthy subjects did not show an effect of lutein on visual acuity or glare sensitivity, that the results of this study were inconsistent as regards contrast sensitivity, and that the evidence provided for a mechanism by which lutein could exert the claimed effect *in vivo* in humans is weak.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of lutein and maintenance of normal vision.

CONCLUSIONS

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

- The food constituent, lutein, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect, which is eligible for further assessment, is maintenance of normal vision. The proposed target population is the general population. Maintenance of normal vision is a beneficial physiological effect.
- The evidence provided is insufficient to establish a cause and effect relationship between the consumption of lutein and maintenance of normal vision.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 for further assessment (No: EFSA-Q-2012-00162, EFSA-Q-2012-00163). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims, references that EFSA has received from Member States or directly from stakeholders and the additional information provided by the competent Authority of Austria for further assessment of this claim (available at: <http://www.efsa.europa.eu/en/topics/topic/article13.htm>).

REFERENCES

- Bernstein PS, Delori FC, Richer S, van Kuijk FJ and Wenzel AJ, 2010. The value of measurement of macular carotenoid pigment optical densities and distributions in age-related macular degeneration and other retinal disorders. *Vision Research*, 50, 716-728.
- Berson EL, Rosner B, Sandberg MA, Weigel-DiFranco C, Brockhurst RJ, Hayes KC, Johnson EJ, Anderson EJ, Johnson CA, Gaudio AR, Willett WC and Schaefer EJ, 2010. Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A. *Archives of Ophthalmology*, 128, 403-411.
- Davies NP and Morland AB, 2004. Macular pigments: their characteristics and putative role. *Progress in Retinal and Eye Research*, 23, 533-559.
- EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2010. Scientific Opinion on the substantiation of health claims related to lutein and maintenance of vision (ID 1603, 1604, 1931) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal*, 8(2):1492, 19 pp.
- EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011. Scientific Opinion on the substantiation of health claims related to lutein and protection of DNA, proteins and lipids from oxidative damage (ID 3427), protection of the skin from UV-induced (including photo oxidative) damage (ID 1605, 1779) and maintenance of normal vision (ID 1779, 2080) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal* 2011;9(4):2030, 16 pp.

- FDA (Food and Drug Administration), 2005. Qualified Health Claims: Letter of Denial - Xangold® Lutein Esters, Lutein, or Zeaxanthin and Reduced Risk of Age-related Macular Degeneration or Cataract Formation (Docket No. 2004Q-0180).
- Kvansakul J, Rodriguez-Carmona M, Edgar DF, Barker FM, Kopcke W, Schalch W and Barbur JL, 2006. Supplementation with the carotenoids lutein or zeaxanthin improves human visual performance. *Ophthalmic and Physiological Optics*, 26, 362-371.
- Ma L, Lin XM, Zou ZY, Xu XR, Li Y and Xu R, 2009. A 12-week lutein supplementation improves visual function in Chinese people with long-term computer display light exposure. *British Journal of Nutrition*, 102, 186-190.
- Rodriguez-Carmona M, Kvansakul J, Harlow JA, Kopcke W, Schalch W and Barbur JL, 2006. The effects of supplementation with lutein and/or zeaxanthin on human macular pigment density and colour vision. *Ophthalmic and Physiological Optics*, 26, 137-147.
- Rodriguez-Rodriguez E, Ortega RM, Lopez-Sobaler AM, Aparicio A, Bermejo LM and Marin-Arias LI, 2006. The relationship between antioxidant nutrient intake and cataracts in older people. *International Journal for Vitamin and Nutrition Research*, 76, 359-366.
- Sasaki M, Yuki K, Kurihara T, Miyake S, Noda K, Kobayashi S, Ishida S, Tsubota K and Ozawa Y, 2011. Biological role of lutein in the light-induced retinal degeneration. *Journal of Nutritional Biochemistry*, 23, 423-429.
- Schalch W, Cohn W, Barker FM, Kopcke W, Mellerio J, Bird AC, Robson AG, Fitzke FF and van Kuijk FJ, 2007. Xanthophyll accumulation in the human retina during supplementation with lutein or zeaxanthin - the LUXEA (LUtein Xanthophyll Eye Accumulation) study. *Archives of Biochemistry and Biophysics*, 458, 128-135.

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 foods⁵ (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 FOOD⁶

Foods are commonly involved in many different functions⁷ 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.

⁵ OJ L12, 18/01/2007

⁶ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁷ 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.

GLOSSARY AND ABBREVIATIONS

AMD	Age-related macular degeneration
ANOVA	Analysis of variance
ARM	Age related maculopathy or macular degeneration
CAT	Contrast acuity thresholds
DNA	Deoxyribonucleic acid
LUXEA	Lutein xanthophyll eye accumulation
MPOD	Macular pigment optical density