SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to conjugated linoleic acid (CLA) isomers and contribution to the maintenance or achievement of a normal body weight (ID 686, 726, 1516, 1518, 2892, 3165), increase in lean body mass (ID 498, 731), increase in insulin sensitivity (ID 1517), protection of DNA, proteins and lipids from oxidative damage (ID 564, 1937), and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination (ID 687, 1519) 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 conjugated linoleic acid (CLA) isomers and contribution to the maintenance or achievement of a normal body weight, increase in lean body mass, increase in insulin sensitivity, protection of DNA, proteins and lipids from oxidative damage, and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination. The scientific

[1] On request from the European Commission, Question No EFSA-Q-2008-1285, EFSA-Q-2008-1351, EFSA-Q-2008-1473, EFSA-Q-2008-1513, EFSA-Q-2008-2253, EFSA-Q-2008-2254, EFSA-Q-2008-2255, EFSA-Q-2008-2670, EFSA-Q-2008-3625, EFSA-Q-2008-3897, adopted on 11 February 2010; Question No EFSA-Q-2008-1518, adopted on 30 April 2010 and Question No EFSA-Q-2008-1474, EFSA-Q-2008-2256, adopted on 10 September 2010.

[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 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 Gut/Immune: Jean-Louis Bresson, Maria Carmen Collado, Miguel Gueimonde, Daisy Jonkers, Martinus Løvik, Bevan Moseley, Maria Saarela, Seppo Salminen, Yolanda Sanz, Stephan Strobel, Daniel Tomé and Hendrik van Loveren. The members of the Claims Sub-Working Group on Weight Management/Satiety/Glucose and Insulin Control/Physical Performance: Kees de Graaf, Joanne Harrold, Mette Hansen, Mette Kristensen, Anders Sjödin and Inge Tetens.

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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 an equimolar mixture of the conjugated linoleic acid (CLA) isomers *c*9, *t*11 and *t*10, *c*12. The Panel considers that an equimolar mixture of the conjugated linoleic acid (CLA) isomers *c*9, *t*11 and *t*10, *c*12, is sufficiently characterised.

Contribution to the maintenance or achievement of a normal body weight

The claimed effect is "weight management", "body weight management" and "weight management, fat metabolism enhancement". The target population is assumed to be the general population. The Panel considers that contribution to the maintenance or achievement of a normal body weight is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that 14 out of 16 intervention studies in humans did not report a significant effect of CLA on body weight, that most of the studies considered were short-term (12 weeks or less), and that none of the three studies on body weight maintenance after weight loss showed a significant effect of CLA compared to placebo.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to the maintenance or achievement of a normal body weight.

Increase in lean body mass

The claimed effect is "supports lean body mass". The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effect relates to an increase in lean body mass. The Panel considers that an increase in lean body mass is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that most of the human studies provided did not observe a significant effect of CLA consumption on lean body mass, and that results from the studies with the largest sample size per intervention group, which used appropriate methods to assess changes in body composition and had an appropriate duration under the proposed conditions of use, are inconsistent with respect to the effects of consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 on lean body mass.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in lean body mass.

Increase in insulin sensitivity

The claimed effect is "insulin sensitivity". The target population is assumed to be the general population. The Panel considers that an increase in insulin sensitivity is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that none of the studies from which conclusions could be drawn for the scientific substantiation of the claimed effect observed a CLA-mediated improvement in insulin sensitivity.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in insulin sensitivity.

Protection of DNA, proteins and lipids from oxidative damage

The claimed effects are "antioxidativity" and "antioxidant capability". The target population is assumed to be the general population. The Panel considers that protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

No human studies which investigated the effects of CLA on markers of oxidative damage to DNA, proteins or lipids have been provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and the protection of DNA, proteins or lipids from oxidative damage.

Contribution to immune defences by stimulation of production of protective antibodies in response to vaccination

The claimed effect is "immune health". The target population is assumed to be the general population. In the context of the proposed wording and the clarifications provided by Member States, the Panel assumes that the claimed effect refers to a contribution to immune defences against pathogens by stimulation of production of protective antibodies in response to vaccination. The Panel considers that contribution to immune defences against pathogens by stimulation of production of protective antibodies in response to vaccination is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that the only study from which conclusions could be drawn for the scientific substantiation of the claim did not report a significant effect of CLA on antibody titres or seroprotection rates after vaccination.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to immune defences against pathogens by stimulation of production of protective antibodies in response to vaccination.

KEY WORDS

Conjugated linoleic acid (CLA), isomers *c*9, *t*11 and *t*10, *c*12, body weight, lean body mass, insulin sensitivity, immune defences, pro-inflammatory, anti-inflammatory cytokines, 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 for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out[5]. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. 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 that is the subject of the health claim is conjugated linoleic acid (CLA).

CLA refers to a group of positional and geometric isomers of linoleic acid that are characterised by the presence of conjugated dienes. CLA is a natural, but minor, component of fats from ruminant animals present in the human diet primarily in meat and dairy products. In nature, the most abundant isomer is *cis*-9, *trans*-11 (*c*9, *t*11), whereas in supplement forms CLA is typically sold as an equal mix of the two predominant isomers *c*9, *t*11 and *t*10, *c*12. Different isomers may have different effects.

The majority of the human intervention studies provided for the scientific substantiation of the health claims have used equimolar combinations of the *c*9, *t*11 and *t*10, *c*12 isomers, and therefore the Panel assumes that the food, which is the subject of the health claims, is an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12

The Panel considers that the food constituent, an equimolar mixture of the conjugated linoleic acid (CLA) isomers *c*9, *t*11 and *t*10, *c*12, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Contribution to the maintenance or achievement of a normal body weight (ID 686, 726, 1516, 1518, 2892, 3165)

The claimed effects are "weight management", "body weight management" and "weight management, fat metabolism enhancement". The Panel assumes that the target population is the general population.

The Panel assumes that the claimed effects refer to contribution to the maintenance or achievement of a normal body weight.

[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] Briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims: http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf

Weight management can be interpreted as contribution to the maintenance of a normal body weight. In this context, weight loss in overweight individuals even without achieving a normal body weight is considered to be a beneficial physiological effect.

The Panel considers that contribution to the maintenance or achievement of a normal body weight is a beneficial physiological effect.

2.2. Increase in lean body mass (ID 498, 731)

The claimed effect is "supports lean body mass". The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effect refers to an increase in lean body mass.

The Panel considers that an increase in lean body mass is a beneficial physiological effect.

2.3. Increase in insulin sensitivity (ID 1517)

The claimed effect is "insulin sensitivity". The Panel assumes that the target population is the general population.

In the context of the proposed wording, the Panel assumes that the claimed effect refers to an increase in insulin sensitivity.

The Panel considers that an increase in insulin sensitivity is a beneficial physiological effect.

2.4. Protection of DNA, proteins and lipids from oxidative damage (ID 564, 1937)

The claimed effects are "antioxidativity" and "antioxidant capability". The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the antioxidant properties of the food component and to the protection of body cells and molecules from oxidative damage caused by free radicals.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation, pollutants). These reactive intermediates damage biologically relevant molecules such as DNA, proteins and lipids if they are not intercepted by the antioxidant network, which includes free radical scavengers such as antioxidant nutrients.

The Panel considers that protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

2.5. Contribution to immune defences by stimulation of production of protective antibodies in response to vaccination (ID 687, 1519)

The claimed effect is "immune health". The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effect refers to the modulation of immune defences against pathogens by

stimulation of production of protective antibodies in response to vaccination, as measured by increased numbers of individuals attaining protective levels of antibodies as well as by increments in antibody titres in groups of individuals.

The Panel considers that contribution to immune defences by stimulation of production of protective antibodies in response to vaccination is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

3.1. Contribution to the maintenance or achievement of a normal body weight (ID 686, 726, 1516, 1518, 2892, 3165)

Most of the randomised, placebo-controlled trials (RCTs) which investigated the effects of CLA supplementation on body weight and body composition in humans that were cited in the consolidated list were included in the meta-analysis by Whigham et al. (2007) described below. One additional RCT not included in the meta-analysis was cited in relation to this claim (Steck et al., 2007).

Whigham et al. (2007) conducted a meta-analysis of randomised, double-blinded, placebo-controlled trials which investigated the effects of interventions using either equimolar mixtures of purified CLA isomers *c*9, *t*11 and *t*10, *c*12 (15 studies, doses ranging from 1g per day to 6.8 g per day, mean dose 3.2 g per day) or purified *t*10, *c*-12 and/or *c*9, *t*11 CLA isomers alone (three studies) on body weight and body composition either during or after weight loss. One of the weight loss studies considered was a 12-month uncontrolled follow-up of a previous 12-month intervention (Gaullier et al., 2005). Most interventions lasted 12 weeks or less. Among the 15 original RCTs which investigated the effects of supplementation with equimolar mixtures of the purified CLA isomers *c*9, *t*11 and *t*10, *c*12 on body weight during weight loss, only two found a significant reduction in body weight in the CLA group compared to the placebo (Watras et al., 2007; Gaullier et al., 2007), whereas no differences between groups were observed in the remaining 13 RCTs (Blankson et al., 2000; Gaullier et al., 2004; Mougios et al., 2001; Smedman and Vessby, 2001; Pinkoski et al., 2006; Berven et al., 2000; Riserus et al., 2002; Malpuech-Brugere et al., 2004; Atkinson, 1999; Petridou et al., 2003; Eyjolfson et al., 2004; Taylor et al., 2006; Lambert et al., 2007). No significant differences in body weight between CLA and the placebo group were observed using either 3.2 g per day CLA or 6.4 g per day CLA (equimolar combination of the *c*9, *t*11 and *t*10, *c*12 isomers) for 12 weeks in the RCT by Steck et al. (2007) which was not included in the meta-analysis.

The meta-analysis by Whigham et al. (2007) also reviewed three studies on the effects of CLA supplementation on body weight maintenance after weight loss (Kamphuis et al., 2003; Larsen et al., 2006; Whigham et al., 2004), none of which observed significant differences between CLA and placebo groups with regard to body weight changes.

In weighing the evidence, the Panel took into account that 14 out of 16 intervention studies in humans did not report a significant effect of CLA on body weight, that most of the studies considered were short-term (12 weeks or less), and that none of the three studies on body weight maintenance after weight loss showed a significant effect of CLA compared to placebo.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to the maintenance or achievement of a normal body weight.

3.2. Increase of lean body mass (ID 498, 731)

Most of the randomised, placebo-controlled trials (RCTs) which investigated the effects of CLA supplementation on body composition in humans that were cited in the consolidated list were included in the meta-analysis by Whigham et al. (2007). One RCT not included in the meta-analysis was also considered by the Panel as pertinent to this claim (Steck et al., 2007). An additional study by Lowery et al. (1998) was available only in abstract form, and could not be fully evaluated by the Panel in relation to the claimed effect.

Among the 15 weight loss RCTs considered in the meta-analysis by Whigham et al. (2007) described in section 3.1, which used an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12, three did not report on changes in lean body mass (Mougios et al., 2001; Smedman and Vessby, 2001; Atkinson, 1999) and nine did not find statistically significant differences between the CLA and control groups in lean body mass changes (Berven et., al., 2000; Eyjolfson et al., 2004; Lambert et al., 2007; Malpuech-Brugere et al., 2004; Petridou et al., 2003; Riserus et al., 2002; Taylor et al., 2006; Gaullier et al., 2007; Watras et al., 2007), whereas three reported an effect of CLA intake on lean body mass during weight loss (Blankson et al., 2000; Gaullier et al., 2004; Pinkoski et al., 2006) in addition to the study by Steck et al. (2007). In the studies by Blankson et al. (2000) and Steck et al. (2007), a significant effect of CLA on lean body mass was observed only at the highest doses of CLA administered (6.8g per day and 6.4g per day of an equal mixture of the *c*9, *t*11 and *t*10, *c*12 CLA isomers, respectively). The Panel notes that these daily doses of CLA are about twice the doses proposed in the conditions of use. The Panel also notes that in the study by Gaullier et al. (2004), the effect was only significant when 3.4 g per day of the CLA isomers, an equal mixture of the *c*9, *t*11 and *t*10, *c*12 isomers, were given as free fatty acids (FFA), but not as triacylglycerols. In addition, only one (Kamphuis et al., 2003) out of the three studies (Kamphuis et al., 2003; Larsen et al., 2006; Whigham et al., 2004) which investigated the effects of CLA supplementation on body composition showed an effect in preserving lean body mass after weight loss independent of physical activity.

The two RCTs with the largest sample size per intervention group and which used appropriate methods to assess body composition and appropriate duration (at least 12 weeks) under the proposed conditions of use (using up to about 3.4g per day of the CLA equimolar mixture) were considered further by the Panel (Gaullier et al., 2004, 2007).

The 108 subjects who participated in the RCT by Gaullier et al. (2004) were selected on the basis of being overweight (BMI 25–30 kg/m^2, age range 18–65 years) and were randomly assigned to consume either 4.5 g olive oil (placebo, n=59, 47 women), 4.5 g 80 % CLA in the FFA form (3.6 g active CLA isomers, equal mixture of the *c*9, *t*11 and *t*10, *c*12, n= 61, 51 women), or 4.5 g 76 % CLA in the triacylglycerol form (3.4 g active CLA isomers, n=60, 51 women) per day for 12 months. Body composition was measured by dual-energy x-ray absorptiometry (DXA). A significant increase in lean body mass was observed only in the CLA-FFA group compared to placebo. No significant differences were observed between the two CLA groups regarding changes in lean body mass during the study. No evidence has been provided to establish that CLA administered as triacylglycerols or as FFA could have differential effects on changes in lean body mass.

The 115 subjects, who participated in another RCT by Gaullier et al. (2007), were selected on the basis of being overweight and obese (BMI 28–32 kg/m^2, age range 18–65 years) and were randomised to consume either 3.4 g per day of the *c*9, *t*11 and *t*10, *c*12 CLA mixture or placebo (4.5 g per day olive oil) for 6 months. Whether the CLA supplement was administered in the FFA form or in the triacylglycerol form was not reported. A total of 105 (84 women) completed the intervention (n=55 in the CLA group), 83 of them with >70 % pill count compliance. No significant changes in lean body mass were observed in the CLA group as compared to placebo in completers or in the subgroup of subjects who reported good compliance.

The Panel notes that the studies by Gaullier et al. (2004, 2007) had similar design and sample size, used the same dose of the CLA equimolar mixture and the same method to assess changes in body composition (dual-energy x-ray absorptiometry), but lead to conflicting results regarding the effects of CLA consumption on lean body mass.

In weighing the evidence, the Panel took into account that most of the human studies provided did not observe a significant effect of CLA consumption on lean body mass, and that results from the studies with the largest sample size per intervention group, which used appropriate methods to assess changes in body composition and had an appropriate duration under the proposed conditions of use, are inconsistent with respect to the effects of consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 on lean body mass.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in lean body mass.

3.3. Increase in insulin sensitivity (ID 1517)

The references provided in the consolidated list for health claims on CLA included six intervention studies in humans, one animal study (*ex vivo*) and one *in vitro* study which were related to the claim (Belury et al., 2003; Moloney et al., 2004, 2007; Riserus et al., 2002; Syvertsen et al., 2007; Smedman and Vessby, 2001; Eyjolfson et al., 2004).

Two double-blind, randomised, control trials (RCTs) were conducted in patients with type 2 diabetes. The study by Belury et al. (2003) did not assess any markers of insulin sensitivity or blood glucose control (but rather changes in body weight and serum leptin) and was therefore not considered pertinent to the claim. In the study by Moloney et al. (2004), 32 subjects with stable, diet-controlled type 2 diabetes were randomly assigned to consume either CLA (3.0 g per day; 50:50 blend of *c*-9, *t*-11 CLA and *t*-10, *c*-12 CLA) or a control fat mix (blend of palm oil and soya bean oil) for eight weeks. A three-hour 75 g oral glucose-tolerance test was performed at baseline and at the end of the intervention to assess insulin sensitivity. CLA supplementation significantly increased fasting glucose concentrations (by 6.3 %; $p<0.05$) and reduced insulin sensitivity as measured by the homeostasis model assessment of insulin resistance (HOMA-IR), the quantitative insulin sensitivity check index (QUICKI) and the insulin sensitivity index (ISI) composite. Fasting insulin concentrations did not change significantly between groups.

Two double-blind RCTs were conducted in obese subjects. In the study by Riserus et al. (2002), a total of 60 abdominally obese men with metabolic syndrome were randomised to consume either 3.4 g per day CLA (equimolar isomer mixture) or placebo for 12 weeks. Insulin sensitivity was assessed by means of the euglycaemic-hyperinsulinaemic clamp. A total of 19 subjects per group entered data analysis. The CLA equimolar isomer mixture did not significantly change glucose metabolism, body composition or body weight compared to placebo. In the study by Syvertsen et al. (2007), 118 subjects were randomly assigned to consume either CLA (3.4 g per day, equal amounts of the *c*9, *t*11 and *t*10, *c*12 isomers) or placebo (4.5 g per day olive oil) for 6 months. Insulin sensitivity was assessed by means of the euglycaemic-hyperinsulinaemic clamp in 41 subjects who completed the study (24 interventions, 17 controls). No significant differences were observed between groups with respect to glucose metabolism, insulin sensitivity or HbA1c during the study.

Two double-blind RCTs were conducted in healthy volunteers. In the study by Smedman and Vessby (2001), 53 healthy men and women aged 23-63 years were randomly assigned to supplementation with CLA (4.2 g per day, equal amounts of the CLA isomers *c*9, *t*11 and *t*10, *c*12), or the same amount of olive oil, during 12 weeks in a double-blind fashion. No significant differences were observed between the groups in fasting plasma insulin or blood glucose. In the study by Eyjolfson et

al. (2004), 16 young sedentary subjects were randomised to consume 4 g per day of mixed CLA isomers (35.5 % *c*-9, *t*-11; 36.8 % *t*-10, *c*-12, n=10), or placebo (safflower oil, n=6) for eight weeks. Oral glucose tolerance tests were performed at baseline, at four and at eight weeks of supplementation. The Panel notes the small sample size of the study, and that direct comparisons between changes in the insulin sensitivity index (ISI) between the intervention and control groups were not reported. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

The animal, *ex vivo*, study showed an effect of *c*9, *t*11-CLA supplementation in down-regulating the insulin receptor substrate 1 (IRS1) and GLUT4 mRNA expression, and an increase in insulin-stimulated glucose transport in 3T3-L1 adipocytes compared with linoleic acid (Moloney et al., 2007), whereas the *in vitro* study reported that the *t*-10, *c*-12 CLA isomer promoted NFkappaB activation and subsequent induction of IL-6, which are at least in part responsible for *t*-10, *c*-12 CLA-mediated insulin-resistance in mature human adipocytes (Chung et al., 2005). The Panel considers that the evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 on the increase in insulin sensitivity in humans.

In weighing the evidence, the Panel took into account that none of the studies from which conclusions could be drawn for the scientific substantiation of the claimed effect observed a CLA-mediated improvement in insulin sensitivity.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in insulin sensitivity.

3.4. Protection of DNA, proteins and lipids from oxidative damage (ID 564, 1937)

Four references were provided in the list in relation to this claim. Two reviews and one intervention study were on the effects of CLA consumption on outcomes unrelated to the claimed effect (e.g. cancer prevention, immune function). The fourth reference reported on an *in vitro* study which assessed the capacity of CLA in scavenging free radicals (Yu, 2001). The Panel notes that the capacity of a food to scavenge free radicals *in vitro* does not predict the occurrence of an effect in the protection of cells or molecules from oxidative damage *in vivo*.

No human studies which investigated the effects of CLA on markers of oxidative damage to DNA, proteins or lipids have been provided.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and the protection of DNA, proteins or lipids from oxidative damage.

3.5. Contribution to immune defences by stimulation of production of protective antibodies in response to vaccination (ID 687, 1519)

Nine references were cited for the substantiation of the claimed effect. These included a narrative review, a poster presentation, two human intervention studies which assessed the effects of CLA isomer mixtures other than the equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 which is the subject of the health claims (Kelley et al., 2000; Tricon et al., 2004), one human study investigating the effects of CLA on outcome measures other than vaccination titres (Song et al., 2005), and three animal studies which addressed the effects of CLA on outcomes unrelated to the claimed effect (Bassaganya-Riera et al. 2001, 2003, 2004). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

One human intervention study was considered pertinent to the claim.

Albers et al. (2003) performed a double-blind, randomised, parallel, controlled study on 71 healthy males (aged 31-69 years) to compare the effects of a 50:50 mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 as free fatty acids (CLA 50:50; 1.7 g per day) to those of an 80:20 mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 as triacylglycerols (CLA 80:20; 1.6 g per day), as compared to a control oil (sunflower oil) on the immune (antibody and cellular) response to a hepatitis B vaccination. The dietary treatment lasted 12 weeks. Subjects received the hepatitis B antigen after 40, 54 and 68 days of treatment. Geometric means of antibody titres, mean integrated lymphocyte stimulation indices or seroprotection rates (i.e. the number of subjects with antibody titres ≥ 10 UI/L) did not differ between groups.

In weighing the evidence, the Panel took into account that the only study from which conclusions could be drawn for the scientific substantiation of the claim did not report a significant effect of CLA on antibody titres or seroprotection rates after vaccination.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination.

CONCLUSIONS

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

- The food constituent, conjugated linoleic acid (CLA) isomers *c*9, *t*11 and *t*10, *c*12, which is the subject of the health claims, is sufficiently characterised.

Contribution to the maintenance or achievement of a normal body weight (ID 686, 726, 1516, 1518, 2892, 3165)

- The claimed effects are "weight management", "body weight management" and "weight management, fat metabolism enhancement". The target population is assumed to be the general population. Contribution to the maintenance or achievement of a normal body weight is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to the maintenance or achievement of a normal body weight.

Maintenance of lean body mass (ID 498, 731)

- The claimed effect is "the support of lean body mass". The target population is assumed to be the general population. An increase in lean body mass is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in lean body mass.

Increase in insulin sensitivity (ID 1517)

- The claimed effect is "insulin sensitivity". The target population is assumed to be the general population. An increase in insulin sensitivity is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and an increase in insulin sensitivity.

Protection of DNA, proteins and lipids from oxidative damage (ID 564, 1937)

- The claimed effects are "antioxidativity" and "antioxidant capability". The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and the protection of DNA, proteins or lipids from oxidative damage.

Contribution to immune defences by stimulation of production of protective antibodies in response to vaccination (ID 687, 1519)

- The claimed effect is "immune health". The target population is assumed to be the general population. The Panel considers that contribution to immune defences by stimulation of production of protective antibodies in response to vaccination is a beneficial physiological effect
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c*9, *t*11 and *t*10, *c*12 and contribution to immune defences by stimulation of production of protective antibodies in response to vaccination.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1285, EFSA-Q-2008-1351, EFSA-Q-2008-1473, EFSA-Q-2008-1474, EFSA-Q-2008-1513, EFSA-Q-2008-1518, EFSA-Q-2008-2253, EFSA-Q-2008-2254, EFSA-Q-2008-2255, EFSA-Q-2008-2256, EFSA-Q-2008-2670, EFSA-Q-2008-3625, EFSA-Q-2008-3897). 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 full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/panels/nda/claims/article13.htm.

REFERENCES

Albers R, van der Wielen RP, Brink EJ, Hendriks HF, Dorovska-Taran VN and Mohede IC, 2003. Effects of cis-9, trans-11 and trans-10, cis-12 conjugated linoleic acid (CLA) isomers on immune function in healthy men. European Journal of Clinical Nutrition, 57, 595-603.

Atkinson RL, 1999. Conjugated linoleic acid for altering body composition and treating obesity. In: Advances in conjugated linoleic acid research. Eds Yurawecz MP, Mossoba MM, Kramer JKG, Pariza MW and Nelson GJ. AOCS Press, Champaign, IL, 348-353.

Bassaganya-Riera J, Hontecillas-Magarzo R, Bregendahl K, Wannemuehler MJ and Zimmerman DR, 2001. Effects of dietary conjugated linoleic acid in nursery pigs of dirty and clean environments on growth, empty body composition, and immune competence. Journal of Animal Science, 79, 714-721.

Bassaganya-Riera J, Pogranichniy RM, Jobgen SC, Halbur PG, Yoon KJ, O'Shea M, Mohede I and Hontecillas R, 2003. Conjugated linoleic acid ameliorates viral infectivity in a pig model of virally induced immunosuppression. Journal of Nutrition, 133, 3204-3214.

Bassaganya-Riera J, Reynolds K, Martino-Catt S, Cui Y, Hennighausen L, Gonzalez F, Rohrer J, Benninghoff AU and Hontecillas R, 2004. Activation of PPAR gamma and delta by conjugated linoleic acid mediates protection from experimental inflammatory bowel disease. Gastroenterology, 127, 777-791.

Belury MA, Mahon A and Banni S, 2003. The conjugated linoleic acid (CLA) isomer, t10c12-CLA, is inversely associated with changes in body weight and serum leptin in subjects with type 2 diabetes mellitus. Journal of Nutrition, 133, 257S-260S.

Berven G, Bye A, Hals O, Blankson H, Fagertun H, Thom E, Wadstein J and Gudmunsen O, 2000. Safety of conjugated linoleic acid (CLA) in overweight or obese human volunteers. European Journal of Lipid Science and Technology, 102, 455-462.

Blankson H, Stakkestad JA, Fagerton H, Thom E, Wadstein J and Gudmundsen O, 2000. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. Journal of Nutrition, 130, 2943-2948.

Chung S, Brown JM, Provo JN, Hopkins R and McIntosh MK, 2005. Conjugated linoleic acid promotes human adipocyte insulin resistance through NFkappaB-dependent cytokine production. Journal of Biological Chemistry, 280, 38445-38456.

Eyjolfson V, Spriet LL and Dyck DJ, 2004. Conjugated linoleic acid improves insulin sensitivity in young, sedentary humans. Medicine and Science in Sports and Exercise, 36, 814 -820.

Gaullier JM, Halse J, Hoye K, Kristiansen K, Fagertun H, Vik H and Gudmundsen O, 2004. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. American Journal of Clinical Nutrition, 79, 1118-1125.

Gaullier JM, Halse J, Hoye K, Kristiansen K, Fagertun H, Vik H and Gudmundsen O, 2005. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. Journal of Nutrition, 135, 778-784.

Gaullier JM, Halse J, Hoivik HO, Hoye K, Syvertsen C, Nurminiemi M, Hassfeld C, Einerhand A, O'Shea M and Gudmundsen O, 2007. Six months supplementation with conjugated linoleic acid induces regional-specific fat mass decreases in overweight and obese. British Journal of Nutrition, 97, 550-560.

Kamphuis MM, Lejeune MP, Saris WH and Westerterp-Plantenga MS, 2003. The effect of conjugated linoleic acid supplementation after weight loss on body weight regain, body composition, and resting metabolic rate in overweight subjects. International Journal of Obesity and Related Metabolic Disorder, 27, 840-847.

Kelley DS, Taylor PC, Rudolph IL, Benito P, Nelson GJ, Mackey BE and Erickson KL, 2000. Dietary conjugated linoleic acid did not alter immune status in young healthy women. Lipids, 35, 1065-1071.

Lambert EV, Goedecke JH, Bluett K, Heggie K, Claassen A, Rae DE, West S, Dugas J, Dugas L, Meltzeri S, Charlton K and Mohede I, 2007. Conjugated linoleic acid versus high-oleic acid sunflower oil: effects on energy metabolism, glucose tolerance, blood lipids, appetite and body composition in regularly exercising individuals. British Journal of Nutrition, 97, 1001-1011.

Larsen TM, Toubro S, Gudmundsen O and Astrup A, 2006. Conjugated linoleic acid supplementation for 1 y does not prevent weight or body fat regain. American Journal of Clinical Nutrition, 83, 606-612.

Lowery LM, Appicelli PA and Lemon PWR, 1998. Conjugated linoleic acid enhances muscle size and strength gains in novice bodybuilders. Medicine and Science in Sports and Exercise, 30, S182.

Malpuech-Brugere C, Verboeket-van de Venne WP, Mensink RP, Arnal MA, Morio B, Brandolini M, Saebo A, Lassel TS, Chardigny JM, Sebedio JL and Beaufrere B, 2004. Effects of two conjugated linoleic Acid isomers on body fat mass in overweight humans. Obesity Research, 12, 591-598.

Moloney F, Toomey S, Noone E, Nugent A, Allan B, Loscher CE and Roche HM, 2007. Antidiabetic effects of cis-9, trans-11-conjugated linoleic acid may be mediated via anti-inflammatory effects in white adipose tissue. Diabetes, 56, 574-582.

Moloney F, Yeow TP, Mullen A, Nolan JJ and Roche HM, 2004. Conjugated linoleic acid supplementation, insulin sensitivity, and lipoprotein metabolism in patients with type 2 diabetes mellitus. American Journal of Clinical Nutrition, 80, 887-895.

Mougios V, Matsakas A, Petridou A, Ring S, Sagredos A, Melissopoulou A, Tsigilis N and Nikolaidis M, 2001. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. Journal of Nutritional Biochemistry, 12, 585-594.

Petridou A, Mougios V and Sagredos A, 2003. Supplementation with CLA: isomer incorporation into serum lipids and effect on body fat of women. Lipids, 38, 805-811.

Pinkoski C, Chilibeck PD, Candow DG, Esliger D, Ewaschuk JB, Facci M, Farthing JP and Zello GA, 2006. The effects of conjugated linoleic acid supplementation during resistance training. Medicine and Science in Sports and Exercise, 38, 339-348.

Riserus U, Arner P, Brismar K and Vessby B, 2002. Treatment with dietary trans10cis12 conjugated linoleic acid causes isomer-specific insulin resistance in obese men with the metabolic syndrome. Diabetes Care, 25, 1516-1521.

Smedman A and Vessby B, 2001. Conjugated linoleic acid supplementation in humans–metabolic effects. Lipids, 36, 773-781.

Song HJ, Grant I, Rotondo D, Mohede I, Sattar N, Heys SD and Wahle KW, 2005. Effect of CLA supplementation on immune function in young healthy volunteers. European Journal of Clinical Nutrition, 59, 508-517.

Steck SE, Chalecki AM, Miller P, Conway J, Austin GL, Hardin JW, Albright CD and Thuillier P, 2007. Conjugated linoleic acid supplementation for twelve weeks increases lean body mass in obese humans. Journal of Nutrition, 137, 1188-1193.

Syvertsen C, Halse J, Hoivik HO, Gaullier JM, Nurminiemi M, Kristiansen K, Einerhand A, O'Shea M and Gudmundsen O, 2007. The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. International Journal of Obesity (Lond), 31, 1148-1154.

Taylor JS, Williams SR, Rhys R, James P and Frenneaux MP, 2006. Conjugated linoleic acid impairs endothelial function. Arteriosclerosis, Thrombosis, and Vascular Biology, 26, 307-312.

Tricon S, Burdge GC, Kew S, Banerjee T, Russell JJ, Grimble RF, Williams CM, Calder PC and Yaqoob P, 2004. Effects of cis-9,trans-11 and trans-10,cis-12 conjugated linoleic acid on immune cell function in healthy humans. American Journal of Clinical Nutrition, 80, 1626-1633.

Watras AC, Buchholz AC, Close RN, Zhang Z and Schoeller DA, 2007. The role of conjugated linoleic acid in reducing body fat and preventing holiday weight gain. International Journal of Obesity , 31, 481–7.

Whigham LD, O'Shea M, Mohede IC, Walaski HP and Atkinson RL, 2004. Safety profile of conjugated linoleic acid in a 12-month trial in obese humans. Food and Chemical Toxicology,42, 1701–9.

Whigham LD, Watras AC and Schoeller DA, 2007. Efficacy of conjugated linoleic acid for reducing fat mass: a meta-analysis in humans. American Journal of Clinical Nutrition, 85, 1203-1211.

Yu L, 2001. Free radical scavenging properties of conjugated linoleic acids. Journal of Agricultural and Food Chemistry, 49, 3452-3456.

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[6] (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[7]

Foods are commonly involved in many different functions[8] 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.

[6] OJ L12, 18/01/2007
[7] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[8] 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 conjugated linoleic acid (CLA) isomers, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
498	CLA (conjugated linoleic acid)	Supports lean body mass	CLA can support lean body mass
	Conditions of use - intake 1.7 - 3.4 g /day - 3.4 g CLA per day - 1,0 g of conjugated linoleic acids/day - Food supplement with 3-6 g of conjugated linoleic acid (CLA) in the daily dose - The product must contain at least 1.5 gram CLA per serving Claim to be used for foods for active individuals - 3600 mg CLA/day - Food supplement with 1.64-3.28g of conjugated linoleic acid (CLA) in the daily dose		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
564	CLA or conjugated linoleic acid	Antioxidativity	Strong plant antioxidant. Antioxidant.
	Conditions of use - Food supplement with 1200-1600 mg of conjugated linoleic acid (CLA) in the daily dose		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
686	Conjugated linoleic acid (CLA)	Weight management	Aids slimming by reducing body fat and preserving lean muscle Helps to reduce muscle protein loss during a diet
	Conditions of use - The product must contain at least 1.5 gram CLA per serving. Claim to be used for foods for active individuals - 1.5-3.4 g CLA/day, CLA is a commercial mixture of 50:50 c10t12 and t9c11 isomers		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
687	Conjugated linoleic acid (CLA)	Immune health	Support of (HepB) vaccine response/Helps respiratory comfort in asthma
	Conditions of use - Up to 3,4 g CLA per day		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
726	Conjugated linoleic acid	Weight management	Helps to reduce muscle protein

	(CLA)		loss during a diet
	Conditions of use - Product-specific claim: 3.4 g CLA per day - 1.5-3.4 g CLA/day, CLA is a commercial mixture of 50:50 c10t12 and t9c11 isomers		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
731	CLA (acido linoleico coniugato) Clarification provided CLA (conjugated linoleic acid)	Aiuta a ridurre il grasso corporeo mantenendo la massa magra. Gli effetti sono: diminuzione della quantità di grasso accumulato dopo i pasti; aumento della lipolisi; aumento del tasso di grasso bruciato nei mitocondri; diminuzione del numero totale di cellule di grasso. Clarification provided Supports lean body mass (intake of CLA reduces body fat and increases lean body mass)	Con acido linoleico coniugato che AIUTA A DIMAGRIRE Clarification provided Conjugated linoleic acid can support lean body mass
	Conditions of use - Aggiunto ad un mix a base di farina per pane		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1516	Conjugated linoleic acid (CLA)	Weight management	Aids slimming by reducing body fat and preserving lean muscle Helps to reduce muscle protein loss during a diet Increases lean tissue mass Increases feelings of fullness and satiety Helps to reduce yoyo-effect after a diet Improves the burning of fat
	Conditions of use - Daily amount to be consumed to produce claimed effect: 95 miligram(s). Length of time after consumption for claimed effect to become apparent: Habitual intake. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: No - 1.5-3.4 g CLA/day, CLA is a commercial mixture of 50:50 c10t12 and t9c11 isomers		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1517	Conjugated linoleic acid (CLA)	Insulin sensitivity	Contributes to healthy blood glucose level
	Conditions of use		

	- Daily amount to be consumed to produce claimed effect: 95 miligram(s). Length of time after consumption for claimed effect to become apparent: Habitual intake. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: No		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1518	Conjugated linoleic acid (CLA) ((cis-9, trans-11 conjugated linoleic acid, and trans-10, cis-12 conjugated linoleic acid (50:50) triglycerides)	Body Weight management	Helps to control fat metabolism Influences lipid metabolism and storage Increases lean muscle mass Reduces body fat percentage Helps to reduce body fat mass while increasing lean body mass Helps to reduce body fat mass Helps to reduce the amount of fat you store after eating Helps to decrease the amount of fat stored in your body Helps to reduce you abdominal fat mass Helps to reduce fat mass in your abdomen and thighs Helps to improve your body shape Helps to increase lean body mass Helps reduce weight gain-helps to reduce SAD (sagittal abdominal diameter)-helps to prevent the yoyo-effect after a diet Helps to reduce muscle protein loss during a diet Helps to increase feelings of fullness and satiety
	Conditions of use - Product-specific claim: 3.4 g CLA per day or intake 1.7 - 3.4 g /day - 3.4 g CLA per day - Daily amount to be consumed to produce claimed effect: 95 miligram(s). Length of time after consumption for claimed effect to become apparent: Habitual intake. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: No - Number of nutrients/other substances that are essential to claimed effect: 4. Names of nutrient/other substances and Quantity in Average daily serving: 50mg CLA, 20mg L-carnitine, 66mg chromium polynicotinate, 300mg garcinia cambogia. Weight of average daily food serving: 150 miligram(s). Daily amount to be consumed to produce claimed effect: 150 miligram(s). Number of food portions this equates to in everyday food portions: 3. Are there factors that could interfere with bioavailability: Yes. Please give reason: do not store above 25 degrees C. Length of time after consumption for claimed effect to become apparent: It is apparent after a period of regular use. Number of days: 14. Is there		

	a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1519	Conjugated linoleic acid (CLA)	Immune health Clarification provided Immune health: Decreases proinflammatory and increased anti-imflammatory cytokines. Increases levels of antibodies. Decreased delayed type hypersensitivity (DTH) response.	Support of (HepB) vaccine response/Helps respiratory comfort in asthma
	Conditions of use - Up to 3,4 g CLA per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1937	CLA (conjugated linoleic acid)	Antioxidant capability	CLA may protect against free radicals
	Conditions of use - The product must contain at least 1.5 gram CLA per serving		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2892	Conjugated Linoleic acid (cis-9, trans-11 and trans-10, cis-12)	weight management, fat metabolism enhancement	helps to control fat metabolism influences lipid metabolism and storage. increases lean muscle mass reduces body fat percentage helps to reduce body fat mass while increasing lean body mass helps to reduce body fat mass helps to reduce the amount of fat you store after eating helps to decrease the amount of fat stored in your body helps to reduce you abdominal fat mass helps to reduce fat mass in your abdomen and thighs helps to improve your body shape helps to increase lean body mass helps reduce weight gain

			helps to reduce SAD (sagittal abdominal diameter) helps to prevent the yoyo-effect after a diet helps to reduce muscle protein loss during a diet helps to increase feelings of fullness and satiety
	Conditions of use - intake 1.7 - 3.4 g /day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3165	Clarinol™	Weight management	Clarinol™ is a unique source of the active form of CLA (conjugated linolenic acid) that reduces the body fat without reducing muscle mass, it reduces subcutaneous fat and the excess weight is gone for good. Clarinol™ prevents fat redeposition (anti yoyo efect). Clarinol™ influences the metabolism speed increase and suppresses its decline particularly at night.
	Conditions of use - The effective dose of CLA is 1.7 g -3.4g/a 50:50 mixture of c9, t11 and t10, c12 is of CLA per day for 12 weeks		

GLOSSARY AND ABBREVIATIONS

BMI	Body mass index
CLA	Conjugated linoleic acid
DXA	Dual-energy x-ray absorptiometry
FFA	Free fatty acids
HOMA-IR	Homeostasis model assessment of insulin resistance
ISI	Insulin sensitivity index)
QUICKI	Quantitative insulin-sensitivity check index
RCT	Randomized controlled trial
ROS	Reactive oxygen species