

SCIENTIFIC OPINION

Scientific Opinion on the safety of “conjugated linoleic acid (CLA)-rich oil” (Clarinol[®]) as a Novel Food ingredient¹

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

European Food Safety Authority (EFSA), Parma, Italy

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SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to carry out the additional assessment for Clarinol[®], conjugated linoleic acid (CLA)-rich oil as a food ingredient in the context of Regulation (EC) No. 258/97 taking account of the comments/objections of a scientific nature raised by the Member States.

Clarinol[®] is manufactured from safflower oil which is used directly or may be subjected to an enzymatic pre-processing to increase the linoleic acid content. Saponification and isomerisation (conjugation) are achieved by subsequent alkaline treatment under reaction conditions resulting in the formation of the *c9,t11* and *t10,c12*-isomers in a ratio of 1:1. Following this isomerisation step, the mixture is diluted and acidified followed by washing, drying and distillation steps. The resulting free fatty acids are re-esterified with glycerol. The single steps of the process are procedures commonly applied in the isolation, refinement and modification of vegetable fats and oils.

Clarinol[®] is intended by the applicant for use as an ingredient in beverages, cereal products, dietary supplements, milk products and dry weight beverages. The intended target consumers are adults. The applicant suggests a daily intake of 3 g CLA, corresponding to approximately 3.75 g Clarinol[®].

¹ On request from the European Commission, Question EFSA-Q-2008-745. Adopted on 30 April 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

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⁴ The EFSA Question number was corrected from EFSA-Q-2009-00745 to EFSA-Q-2008-745 and line numbers were deleted.

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The average intake of naturally occurring CLA from food is estimated to be about 0.3 g/day in Europe. A supplementation of 3 g CLA would therefore lead to a 10-fold increase in CLA intake. However the most abundant CLA isomer naturally occurring in foods is the *c9,t11* isomer, accounting for more than 90 % of the dietary CLA intake. Thus an intake of 3 g CLA from Clarinol[®] with a *c9,t11*: *t10,c12* ratio of 1:1 would lead to an approximately 6-fold increase of the intake of *c9,t11* isomer, and a 50-fold increase of the *t10,c12*-isomer.

The applicant provided data from animal studies on absorption, distribution, metabolism and excretion. The metabolism follows standard pathways known for fatty acids consumed as triglycerides. A number of non-human studies have been provided on the acute, subchronic, chronic, geno-, reproductive, and developmental toxicity and carcinogenicity of CLA. The available data from non-human studies do not indicate a risk for genotoxicity, reproductive toxicity, carcinogenicity or allergenicity.

In addition non-human studies were provided on the effects of CLA on lipid metabolism parameters, hepatic lipid accumulation, liver function, markers of inflammation, insulin sensitivity and glucose metabolism. *In vitro* data suggest that the *t10,c12* CLA isomer is involved in the regulation of fatty acid synthesis and mediating suppression of insulin sensitivity in mature human adipocytes. This isomer has also been reported to be responsible for undesirable effects on fat and glucose metabolism *in vivo*. Mice seem to be particularly sensitive to the effects of CLA on fat and glucose metabolism. However the extent of the effects of CLA on insulin resistance and also on markers of cardiovascular risk appears to be species-dependent. Therefore the focus of the safety assessment relies mainly on human studies.

The administration of the 1:1 isomer mixture of CLA to normal weight, overweight and obese non-diabetic subjects does not appear to have adverse effects on insulin sensitivity, blood glucose control or liver function at the proposed conditions of use up to six months. Effects of CLA consumption over periods longer than six months on insulin sensitivity and liver steatosis have not been adequately addressed in humans. With respect to type-2 diabetic subjects, the evidence provided does not establish the safety of CLA under the proposed conditions of use, since the CLA 1:1 isomer mixture appears to adversely affect both static (HOMA-IR) and dynamic (ISI, OGIS) surrogate markers of insulin sensitivity as well as fasting blood glucose and no studies on blood glucose control (e.g., HbA1c) are available for periods of consumption beyond eight weeks. Under the proposed conditions of use, CLA has no effect on LDL-cholesterol concentrations or the LDL:HDL-cholesterol ratio, and the magnitude of the changes observed in HDL- and triglyceride concentrations are unlikely to have an impact on cardiovascular risk. However, the observed increase in plasma and urinary concentrations of isoprostanes, which may indicate an increase in lipid peroxidation, and the increase in some markers of subclinical inflammation (i.e., 15-*keto*-dihydroprostaglandin F_{2α} and possibly C-reactive protein associated to CLA consumption, together with the limited data available on the effects of CLA on vascular function may indicate a potential for vascular damage (i.e., atherosclerosis) in the longer term. No data on effects of CLA intake on the arterial wall have been provided in humans.

The Panel considers that CLA consumption does not appear to have adverse effects on insulin sensitivity, blood glucose control or liver function for up to six months, and that observed effects on blood lipids are unlikely to have an impact on cardiovascular risk. Long-term effects of CLA intake on insulin sensitivity and the arterial wall have not been adequately addressed in humans. The evidence provided does not establish the safety of CLA consumption by type-2 diabetic subjects under the proposed conditions of use.

The Panel concludes that the safety of Clarinol[®], an oil with approximately 80 % CLA 1:1 mixture of *t9,c11* and *t10,c12* isomers, has been established for the proposed uses at intakes of 3.75 g Clarinol[®] per day (corresponding to 3 g CLA), for up to six months. The safety of CLA consumption for periods

longer than six months has not been established under the proposed conditions of use. The safety of CLA consumption by type-2 diabetic subjects has not been established.