

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations pursuant to Article 13(5) 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 an application from Sylvan Bio Europe BV, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the Netherlands, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations. The food, monacolin K in SYLVAN BIO red yeast rice, that is the subject of the health claim is sufficiently characterised. The claimed effect, maintenance of normal blood LDL-cholesterol concentrations, is a beneficial physiological effect. A claim on monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome at daily intakes of 10 mg monacolin K from any red yeast rice preparation (which would include SYLVAN BIO red yeast rice). The evidence provided by the applicant for the present application does not establish that monacolin K in SYLVAN BIO red yeast rice is different from monacolin K in other red yeast rice preparations with respect to its effect on blood LDL-cholesterol concentrations.

© European Food Safety Authority, 2013

KEY WORDS

Red yeast rice, Sylvan Bio, monacolin K, LDL-cholesterol, health claims.

¹ On request from the Competent Authority of the Netherlands following an application by Sylvan Bio Europe BV, Question No EFSA-Q-2012-00736, adopted on 24 January 2013.

² Panel members: Carlo Agostoni, Roberto Berni Canani, Susan Fairweather-Tait, Marina Heinonen, Hannu Korhonen, Sébastien La Vieille, Rosangela Marchelli, Ambroise Martin, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Sean (J.J.) Strain, Inge Tetens, Daniel Tomé, Dominique Turck and Hans Verhagen. Correspondence: nda@efsa.europa.eu

³ Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Hildegard Przyrembel, Yolanda Sanz, Alfonso Siani, Sean (J.J.) Strain, Inge Tetens, Dominique Turck, Hendrik Van Loveren, Hans Verhagen and Peter Willatts for the preparatory work on this scientific opinion.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations pursuant to Article 13(5) of Regulation (EC) No 1924/2006. EFSA Journal 2013;11(2):3084. [13 pp.]. doi:10.2903/j.efsa.2013.3084. Available online: www.efsa.europa.eu/efsajournal

SUMMARY

Following an application from Sylvan Bio Europe BV, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the Netherlands, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The application included a request for the protection of proprietary data.

The food that is the subject of the health claim is SYLVAN BIO red yeast rice. The Panel notes that the major active constituent in SYLVAN BIO red yeast rice is monacolin K (hydroxyacid and lactone forms). The Panel considers that the food constituent, monacolin K in SYLVAN BIO red yeast rice, is sufficiently characterised.

The claimed effect is “maintenance of blood LDL-cholesterol concentrations”. The target population proposed by the applicant is “adults in the general population who want to control their blood cholesterol”. The Panel considers that maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.

A claim on monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome. The conditions of use for this claim foresee a daily intake of 10 mg monacolin K from any red yeast rice preparation (which would include SYLVAN BIO red yeast rice) in order to obtain the claimed effect.

The present application refers to a claim on monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations.

The applicant identified in a literature search one published randomised controlled trial (RCT) and provided in addition one unpublished RCT which investigated the effect of monacolin K in SYLVAN BIO red yeast rice on blood LDL-cholesterol concentrations compared to placebo. The applicant also identified through the literature search one RCT on the effects of monacolin K in SYLVAN BIO red yeast rice on blood LDL-cholesterol concentrations relative to pravastatin (positive control), which was provided as supportive evidence for the scientific substantiation of the claim.

The Panel notes that out of these three studies, one study showed an effect of monacolin K in SYLVAN BIO red yeast rice on blood LDL-cholesterol concentrations at doses of about 9 mg per day, that a second study showed an effect of monacolin K in SYLVAN BIO red yeast rice at doses of about 10 mg per day, and that a third study supports an effect of monacolin K in SYLVAN BIO red yeast rice at doses of about 14 mg per day. The Panel also notes the uncertainties regarding the amount of monacolin K in SYLVAN BIO red yeast rice, and that the amount of monacolin K used in the studies provided for the scientific substantiation of this claim is in the range (or above) the doses used in the two human intervention studies which were evaluated by the Panel to set conditions of use of 10 mg monacolin K per day for a claim on monacolin K from red yeast rice preparations in general and maintenance of normal blood LDL-cholesterol concentrations.

The Panel considers that the evidence provided by the applicant does not establish that monacolin K in SYLVAN BIO red yeast rice is different from monacolin K in other red yeast rice preparations with respect to its effect on blood LDL-cholesterol concentrations.

The Panel concludes that a cause and effect relationship has been established between the consumption of monacolin K in red yeast rice preparations, which include SYLVAN BIO red yeast rice, and maintenance of normal blood LDL-cholesterol concentrations.

The Panel could have reached this conclusion without the human intervention study claimed as proprietary by the applicant.

The Panel considers that the following wording reflects the scientific evidence: “Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol concentrations”.

The Panel considers that in order to obtain the claimed effect, 10 mg of monacolin K from fermented red yeast rice preparations should be consumed daily. The target population is adults in the general population.

In relation to restrictions of use, the Panel refers to the Summary of Product Characteristics of lovastatin-containing medicinal products available on the EU market.

The Panel also refers to the opinion by the EFSA CONTAM Panel on citrinin (a nephrotoxic mycotoxin) which can be produced by some strains of *Monascus purpureus*.

TABLE OF CONTENTS

Abstract	1
Summary	2
Table of contents	4
Background	5
Terms of reference	5
EFSA Disclaimer.....	6
Information provided by the applicant	7
Assessment	7
1. Characterisation of the food/constituent	7
2. Relevance of the claimed effect to human health.....	8
3. Scientific substantiation of the claimed effect	8
4. Panel’s comments on the proposed wording	11
5. Conditions and restrictions of use	11
Conclusions	11
Documentation provided to EFSA	12
References	12
Glossary and Abbreviations	13

BACKGROUND

Regulation (EC) No 1924/2006⁴ harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA

- The application was received on 23/07/2012.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The application included a request for the protection of proprietary data.
- On 08/08/2012, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 11/09/2012, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 25/09/2012.
- On 25/10/2012, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The clock was stopped on 30/10/2012 and restarted on 14/11/2012, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 20/11/2012, EFSA received the requested information (which was made available to EFSA in electronic format on 12/11/2012).
- During its meeting on 24/01/2013, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations.

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.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of SYLVAN BIO red yeast rice, a positive assessment of its safety, nor a decision on whether SYLVAN BIO red yeast rice is, or is not, classified as a foodstuff. 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 wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: Sylvan Bio Europe BV, Venrayseweg 132/a, 5961 NT Horst, the Netherlands.

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006 (Myers et al., 2006, unpublished).

Food/constituent as stated by the applicant

According to the applicant, the food which is the subject of the claim is SYLVAN BIO red yeast rice, which is a fermented product of rice on which "red yeast" (*Monascus purpureus*) has been grown.

Health relationship as claimed by the applicant

According to the applicant, the health relationship is related to the maintenance of blood LDL-cholesterol concentrations.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "A daily intake of at least 2.4 g of SYLVAN BIO red yeast rice, corresponding to 4.08 mg of monacolin K, contributes to the maintenance of normal blood LDL-cholesterol."

Specific conditions of use as proposed by the applicant

According to the applicant, the target population is adults in the general population who want to control their blood cholesterol. The applicant has proposed an intake of SYLVAN BIO red yeast rice equivalent to 4.08 mg/day of monacolin K.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claim is SYLVAN BIO red yeast rice.

Red yeast rice (RYR) is produced by fermentation of rice with the fungus *Monascus purpureus*. Preparations of RYR typically contain starch, protein, fat (including monounsaturated fatty acids, plant sterols), isoflavones, and other compounds. Depending on the *Monascus* strains used and the fermentation conditions, the preparations may contain polyketides called monacolins, which are secondary metabolites produced during fermentation (Liu et al., 2006). Monacolin K has been specified as the food constituent in RYR preparations which is responsible for the claimed effect.

The RYR preparation, SYLVAN BIO RYR, which is the subject of the claim, is dried and milled after fermentation and contains around 0.4 % monacolin K (MK) calculated as the sum of monacolin K in the lactone form (MKL; also known as lovastatin or mevinolin), hydrolysed monacolin K (hydroxyacid form, frequently referred to as monacolin KA (MKA)), and dehydromonacolin K. Active monacolin K (hydroxyacid and lactone forms (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011)) amounts to 84 to 98 % of the monacolin K forms in the three batches for which analytical data were provided. The Panel notes that the major active constituent in SYLVAN BIO RYR is monacolin K (hydroxyacid and lactone forms).

Information about the manufacturing process, the stability and the batch-to-batch variability has been provided. Monacolin K is measurable in foods by established methods.

The Panel considers that the food constituent, monacolin K in SYLVAN BIO red yeast rice, which is the subject of the claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is “maintenance of blood LDL-cholesterol concentrations”. The target population proposed by the applicant is “adults in the general population who want to control their blood cholesterol”.

Low-density lipoproteins (LDL) carry cholesterol to peripheral tissues, including the arteries. Elevated LDL-cholesterol, by convention >160 mg/dL (>4.1 mmol/L), may compromise the normal structure and function of the arteries.

The Panel considers that maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

A claim on monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011). The conditions of use for this claim foresee a daily intake of 10 mg monacolin K from any red yeast rice preparation (which would include SYLVAN BIO RYR) in order to obtain the claimed effect.

The outcome of the previous assessment, including the conditions of use, was based on the evidence provided by two human intervention studies (Heber et al., 1999; Lin et al., 2005) which investigated the effect of two different RYR preparations (other than SYLVAN BIO RYR) on LDL-cholesterol concentrations at doses of about 7.5 mg/day (MKL+MKA) and 11.5 mg/day (MKL), respectively; on the well-known mechanism of action of pure monacolin K (lovastatin) for the effect (inhibition of HMG-CoA reductase); and on the lowest dose of pure monacolin K which has been shown consistently to reduce LDL-cholesterol concentrations in the target population (10 mg/day).

The present application refers to a claim on monacolin K in SYLVAN BIO RYR and maintenance of normal blood LDL-cholesterol concentrations.

The applicant performed a literature search in Medline up to December 2011 using the following key words for search in titles and abstracts: (“red yeast rice” OR “*Monascus purpureus*”) AND (“cholesterol” OR “blood lipid” OR “low-density lipoprotein cholesterol” OR “LDL-cholesterol”) to identify randomised controlled trials (RCTs) in normo- and mildly hypercholesterolaemic subjects not on blood lipid lowering medication with a duration of at least eight weeks and assessing the effect of red yeast rice preparations on changes in blood LDL-cholesterol concentrations. The search was limited to human studies published in English. In addition, hand searches were performed.

The applicant identified through the literature search one published RCT (Becker et al., 2009) and provided in addition one unpublished RCT (Myers et al., 2006, unpublished, claimed as proprietary by the applicant) which investigated the effect of monacolin K in SYLVAN BIO RYR on blood LDL-cholesterol concentrations compared to placebo. The applicant also identified through the literature search one RCT on the effect of monacolin K in SYLVAN BIO RYR on blood LDL-cholesterol concentrations relative to pravastatin (positive control), which was provided as supportive evidence for the scientific substantiation of the claim (Halbert et al., 2010).

In a randomised, double-blind, placebo-controlled, three-arm parallel study (Myers et al., 2006, unpublished, claimed as proprietary) 85 subjects (48 female) with hypercholesterolaemia and who were not on lipid lowering medication were randomised to consume daily either 2.4 g of SYLVAN BIO RYR (n=31), 1.2 g of SYLVAN BIO RYR (n=28) or an unknown placebo (n=26) for 12 weeks. The applicant claimed that 2.4 g of SYLVAN BIO RYR contained 4.08 mg of monacolin K, and that 1.2 g of SYLVAN BIO RYR contained 2.04 mg of monacolin K. The Panel notes that the content of monacolin K of the RYR used in this study was not reported in the original unpublished report, and that the content of monacolin K in 2.4 g and 1.2 g of SYLVAN BIO RYR, when considering the information provided for the characterisation of SYLVAN BIO RYR, should have been higher than 4.08 mg and 2.04 mg, respectively. Upon a request from EFSA, the applicant clarified that the RYR preparation used in this study complied with the specifications provided for SYLVAN BIO RYR, and that, taking into account all the active forms, 2.4 g and 1.2 g of SYLVAN BIO RYR, contained 8.96 mg and 4.48 mg of monacolin K, respectively.

LDL-cholesterol concentrations were measured at baseline and at weeks 4, 8 and 12. It was estimated that 24 subjects per arm were needed to detect an 11.5 % difference in blood LDL-cholesterol concentration changes between groups with 80 % power and $\alpha=0.05$, allowing for a 15 % attrition rate. Two subjects were excluded prior to the start of the intervention for not meeting the inclusion criteria. A total of 13 subjects dropped out during the study and another subject was not considered in the analysis owing to an incomplete dataset for LDL-cholesterol measurements. Reasons for drop-outs were reported. The analysis was carried out on the sample of completers (23 in the 2.4 g group, 25 in the 1.2 g group and 26 in the placebo group) using a two-way repeated measures analysis of variance (RM-ANOVA) with treatment and time as factors. There was a statistically significant visit x treatment interaction for changes in LDL-cholesterol concentrations from baseline to week 12 between groups ($p=0.001$). Pair-wise comparisons between groups at this time point, adjusted by the Bonferroni correction, showed a significant reduction in LDL-cholesterol in the 2.4 g SYLVAN BIO RYR group compared to placebo ($p<0.0001$), while no differences were observed between the 1.2 g SYLVAN BIO RYR group and placebo.

The Panel notes that drop-outs were not taken into account in data analysis. The Panel considers that this study with some methodological limitations shows an effect of monacolin K in SYLVAN BIO RYR on blood LDL-cholesterol concentrations at doses of about 9 mg per day, but it does not show an effect of monacolin K in SYLVAN BIO RYR at doses of about 4.5 mg per day.

In a double-blind, randomised, placebo-controlled parallel trial (Becker et al., 2009), 62 statin-intolerant hypercholesterolaemic subjects were randomised in blocks of four, stratified by baseline LDL-cholesterol concentrations, to consume daily either six capsules of SYLVIAN BIO RYR (n=31) or an unknown placebo (n=31) for 24 weeks. Capsules of SYLVIAN BIO RYR were purchased in the market by the investigators and their content of monacolin K was analysed by an independent laboratory. Six capsules (daily dose) of SYLVIAN BIO RYR contained 3.6 g of the product and 9.8 mg of monacolin K. The Panel notes that the amount of monacolin K per gram of SYLVIAN BIO RYR was lower than that specified by the applicant in the characterisation of the product and that used in the study by Myers et al. (2006, unpublished).

The primary outcome of the study was LDL-cholesterol concentrations at weeks 12 and 24 of the study. Two subjects dropped out in the placebo group and one in the intervention group (reasons for drop-outs reported). Data were analysed using a linear mixed effects model with treatment and time as factors. A significant decrease in LDL-cholesterol concentrations was observed in the intervention group compared to placebo at week 12 (-0.92 mmol/L 95 % CI -1.36 to -0.48) and week 24 (-0.56 mmol/L, 95 % CI -1.0 to -0.13) of the study. The Panel notes that drop-outs were not taken into account in data analysis. The Panel considers that this study with some methodological limitations shows an effect of monacolin K in SYLVIAN BIO RYR at doses of about 10 mg per day.

In a randomised, double-blind, controlled, parallel study (Halbert et al., 2010), 43 statin-intolerant hypercholesterolaemic subjects were randomised in blocks of four to consume daily either SYLVAN BIO RYR or 40 mg pravastatin (positive control) for 12 weeks. Capsules of SYLVAN BIO RYR were purchased in the market by the investigators and their content of monacolin K was analysed by an independent laboratory. Eight capsules (daily dose) of SYLVAN BIO RYR contained 4.8 g of the product and 14.28 mg of monacolin K. The Panel notes that the amount of monacolin K per gram of SYLVAN BIO RYR was lower than that specified by the applicant in the characterisation of the product and than that used in the study by Myers et al. (2006, unpublished).

The primary outcome of the study was the rate of withdrawal from treatment because of intolerable muscle pain. Change in blood LDL-cholesterol concentrations was a secondary outcome. Data were analysed using a linear regression model with baseline LDL-cholesterol concentrations and baseline body mass index as covariates. Two subjects in the SYLVAN BIO RYR group and four in the pravastatin group discontinued the study. Changes in LDL-cholesterol concentrations were not significantly different between the SYLVAN BIO RYR and the pravastatin groups. The Panel considers that this study supports an effect of monacolin K in SYLVAN BIO RYR on LDL-cholesterol concentrations at doses of about 14 mg per day.

As supportive evidence, the applicant also provided 20 human intervention studies on RYR preparations other than SYLVAN BIO RYR, one meta-analysis of human intervention studies using various RYR preparations, one retrospective analysis on the association of use of RYR preparations and blood cholesterol concentrations, and 10 narrative reviews, two systematic reviews and one book chapter on RYR preparations. The applicant also provided a number of references in support of the mechanism by which RYR preparations exert an effect on blood LDL-cholesterol concentrations through monacolin K activity. The Panel considers that these references do not provide information on the effects of monacolin K in SYLVAN BIO RYR on the maintenance of blood LDL-cholesterol concentrations.

The Panel notes that one study (Myers et al., 2006, unpublished) showed an effect of monacolin K in SYLVAN BIO RYR on blood LDL-cholesterol concentrations at doses of about 9 mg per day, that a second study (Becker et al., 2009) showed an effect of monacolin K in SYLVAN BIO RYR at doses of about 10 mg per day, and that a third study (Halbert et al., 2010) supports an effect of monacolin K in SYLVAN BIO RYR at doses of about 14 mg per day. The Panel also notes the uncertainties underlying the amount of monacolin K in SYLVAN BIO RYR, and that the amount of monacolin K used in the studies (Becker et al., 2009; Halbert et al., 2010; Myers et al., 2006, unpublished) provided for the scientific substantiation of this claim is in the range (or above) the doses used in the two human intervention studies (Heber et al., 1999; Lin et al., 2005) which were evaluated by the Panel to set conditions of use of 10 mg monacolin K per day for a claim on monacolin K from RYR preparations in general and maintenance of normal blood LDL-cholesterol concentrations (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011).

The Panel considers that the evidence provided by the applicant does not establish that monacolin K in SYLVAN BIO RYR is different from monacolin K in other red yeast rice preparations with respect to its effect on blood LDL-cholesterol concentrations.

The Panel concludes that a cause and effect relationship has been established between the consumption of monacolin K in red yeast rice preparations, which include SYLVAN BIO red yeast rice, and maintenance of normal blood LDL-cholesterol concentrations.

A claim on monacolin K from red yeast rice and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011).

The Panel could have reached this conclusion without the human intervention study claimed as proprietary by the applicant (Myers et al., 2006, unpublished).

4. Panel's comments on the proposed wording

The Panel considers that the following wording reflects the scientific evidence: "Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol concentrations".

5. Conditions and restrictions of use

The Panel considers that in order to obtain the claimed effect, 10 mg of monacolin K from fermented red yeast rice preparations should be consumed daily. The target population is adults in the general population.

In relation to restrictions of use, the Panel refers to the Summary of Product Characteristics of lovastatin-containing medicinal products available on the EU market.

The Panel also refers to the opinion by the EFSA CONTAM Panel on citrinin (a nephrotoxic mycotoxin) which can be produced by some strains of *Monascus purpureus* (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2012).

CONCLUSIONS

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

- The food constituent, monacolin K in SYLVAN BIO red yeast rice, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is "maintenance of blood LDL-cholesterol concentrations". The target population proposed by the applicant is "adults in the general population who want to control their blood cholesterol". Maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.
- The Panel concludes that a cause and effect relationship has been established between the consumption of monacolin K in red yeast rice preparations, which include SYLVAN BIO red yeast rice, and maintenance of normal blood LDL-cholesterol concentrations.
- The following wording reflects the scientific evidence: "Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol concentrations".
- In order to obtain the claimed effect, 10 mg of monacolin K from fermented red yeast rice preparations should be consumed daily. The target population is adults in the general population.
- In relation to restrictions of use, reference is made to the Summary of Product Characteristics of lovastatin-containing medicinal products available on the EU market and to the opinion by the EFSA CONTAM Panel on citrinin (a nephrotoxic mycotoxin) which can be produced by some strains of *Monascus purpureus*.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on monacolin K in SYLVAN BIO red yeast rice and maintenance of normal blood LDL-cholesterol concentrations pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0361_NL). September 2012. Submitted by Sylvan Bio BV.

REFERENCES

- Becker DJ, Gordon RY, Halbert SC, French B, Morris PB and Rader DJ, 2009. Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial. *Annals of Internal Medicine*, 150, 830-839, W147-839.
- EFSA Panel on Contaminants in the Food Chain (CONTAM), 2012. Scientific Opinion on the risks for public and animal health related to the presence of citrinin in food and feed. *EFSA Journal*, 10(3):2605, 82 pp.
- EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011. Scientific Opinion on the substantiation of health claims related to monacolin K from red yeast rice and maintenance of normal blood LDL cholesterol concentrations (ID 1648, 1700) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal*, 9(7):2304, 16 pp.
- Halbert SC, French B, Gordon RY, Farrar JT, Schmitz K, Morris PB, Thompson PD, Rader DJ and Becker DJ, 2010. Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. *American Journal of Cardiology*, 105, 198-204.
- Heber D, Yip I, Ashley JM, Elashoff DA, Elashoff RM and Go VL, 1999. Cholesterol-lowering effects of a proprietary Chinese red-yeast-rice dietary supplement. *American Journal of Clinical Nutrition*, 69, 231-236.
- Lin CC, Li TC and Lai MM, 2005. Efficacy and safety of *Monascus purpureus* Went rice in subjects with hyperlipidemia. *European Journal of Endocrinology*, 153, 679-686.
- Liu J, Zhang J, Shi Y, Grimsgaard S, Alraek T and Fonnebo V, 2006. Chinese red yeast rice (*Monascus purpureus*) for primary hyperlipidemia: a meta-analysis of randomized controlled trials. *Chinese Medicine*, 1, 4.
- Myers SP, Cheras PA, Brooks L and O'Connor J, 2006, unpublished. Study on the Safety and Efficacy of Sylvan Red Yeast Rice in Adults with Primary Hypercholesteremia (claimed as proprietary by the applicant).

GLOSSARY AND ABBREVIATIONS

HMG-CoA reductase	Hydroxy-Methyl Glutaryl Coenzyme A reductase
LDL	Low density lipoprotein
MK	Monacolin K (sum of MKA+MKL)
MKA	Monacolin K, hydroxyacid form
MKL	Monacolin K, lactone form
RCT	Randomised controlled trial
RM-ANOVA	Repeated measures analysis of variance
RYR	Red yeast rice