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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to "*Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type 'heart cheese' of Harmony™" and maintenance of normal blood pressure pursuant to Article 13(5) of Regulation (EC) No 1924/2006[1]

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

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ABSTRACT

Following an application from E-piim production Ltd, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Estonia, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to "*Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type "heart cheese" of Harmony™" and maintenance of normal blood pressure (BP). The food constituent *L. plantarum* TENSIA®, which is the subject of the health claim, is sufficiently characterised. The Panel considers that the maintenance of normal blood pressure is a beneficial physiological effect. The applicant provided 47 references which did not address the effects of *L. plantarum* TENSIA® on BP. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim. Two human randomised, double-blind, placebo-controlled, intervention studies investigated the effect on BP of *L. plantarum* TENSIA® consumed in Edam-type cheese for three and eight weeks. In weighing the evidence, the Panel took into account that only one human intervention study with important methodological limitations showed a BP-lowering effect of *L. plantarum* TENSIA® consumed in the Edam-type "heart cheese" of Harmony™ when consumed daily for eight weeks, and that no evidence was provided for a mechanism by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert the claimed effect. The Panel concludes that a cause and effect relationship has not been established between the consumption of *Lactobacillus plantarum* TENSIA®in the semi-hard Edam-type "heart cheese" of Harmony™ and maintenance of normal blood pressure.

KEY WORDS

Lactobacillus plantarum TENSIA®, cheese, blood pressure, health claims

[1] On request from the Competent Authority of Estonia following an application by E-piim production Ltd, Question No EFSA-Q-2014-00097, adopted on 18 September 2014.

[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. One member of the Panel did not participate in the discussion on the subject referred to above because of potential conflicts of interest identified in accordance with the EFSA policy on declarations of interests. 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, Hendrik Van Loveren, Hans Verhagen and Peter Willatts for the preparatory work on this scientific opinion.

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SUMMARY

Following an application from E-piim production Ltd, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Estonia, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to "*Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type "heart cheese" of Harmony™" and maintenance of normal blood pressure.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The food constituent that is the subject of the health claim is *L. plantarum* TENSIA® in the semi-hard Edam-type "heart cheese" of Harmony™. The strain *L. plantarum* TENSIA® (DSM 21380) has been specified using phenotypic and genotypic methods. Data on the conditions of use, specifications, manufacturing process and bioavailability as well as information on the stability of the strain were provided. The Panel considers that *L. plantarum* TENSIA®, the food constituent which is the subject of the health claim, is sufficiently characterised.

The claimed effect proposed by the applicant is "maintenance of cardio-vascular health through reduction of blood pressure". The target population proposed by the applicant is the general population. The Panel notes that the claimed effect relates to the maintenance of normal blood pressure. The Panel considers that the maintenance of normal blood pressure is a beneficial physiological effect.

The applicant provided 47 (27 human and 20 non-human) references which included human intervention studies, guidelines, narrative reviews, and *in vitro* studies that did not address the effects of *L. plantarum* TENSIA® on blood pressure (BP). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

Two human randomised, double-blind, placebo-controlled, intervention studies investigated the effect of *L. plantarum* TENSIA® consumed in Edam-type cheese for three and eight weeks on BP. In the eight-week study, 136 participants who fulfilled the inclusion criteria at screening were randomised to consume Edam-type cheese with or without *L. plantarum* TENSIA®. The Panel notes that 35 participants among those randomised did not fulfil the inclusion/exclusion criteria at baseline. Between-group differences in long-term (eight weeks) change in systolic blood pressure (SBP) (primary outcome), in long-term change in diastolic blood pressure (DBP), and in short-term (one to four weeks and five to eight week) changes in SBP and DBP were analysed in different populations (i.e. intention to treat (ITT), "modified-ITT" (mITT), and per protocol (PP) populations). SBP significantly decreased in the test group compared with the control group from baseline to week 8 in the mITT, ITT and PP populations. Data were also analysed by a mixed model using the mixed procedure in SAS and selecting an unstructured covariance structure. In the ITT population a statistically significant treatment by time interaction between groups was observed for SBP and DBP from baseline to week 8, whereas no statistically significant effect of treatment over time was observed in the PP population for both SBP and DBP from baseline to week 8.

The Panel notes that the different results obtained in the ITT, mITT and PP populations using the statistical analyses above can be explained by the low proportion of randomised participants who completed the protocol as planned in relation to the primary outcome (60 out of 136, 44 %), and this is an important limitation of the study, together with the fact that 35 of the randomised participants did not meet the inclusion criteria at baseline. The Panel considers that this study with important methodological limitations shows a blood pressure-lowering effect of *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ when consumed daily for eight weeks.

In the three-week cross-over study, which had already been submitted in a previous application for the same claim, 90 participants were randomised to consume Edam-type cheese with or without *L. plantarum* TENSIA® and 83 participants completed the trial. Changes in SBP and DBP were the primary outcomes of the study. No significant differences in SBP or DBP changes were observed between the intervention and control groups during the study. The Panel notes that this study does not show an effect of *L. plantarum* TENSIA® in Edam-type cheese on BP when consumed for three weeks.

The applicant indicated that the mechanisms by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert an effect on BP are probably complex and mainly related to the ability of the strain to produce metabolites (i.e. acetylcholine, angiotensin-converting enzyme-inhibitory peptides, nitric oxide) with vasodilation activity. The applicant provided three unpublished *in vitro* studies and a patent to support the proposed mechanisms for the claimed effect. The Panel notes that no evidence was provided by the applicant for a mechanism by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert the claimed effect.

In weighing the evidence, the Panel took into account that only one human intervention study with important methodological limitations showed a BP-lowering effect of *L. plantarum* TENSIA® consumed in the Edam-type "heart cheese" of Harmony™ when consumed daily for eight weeks, and that no evidence was provided for a mechanism by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of *Lactobacillus plantarum* TENSIA®in the semi-hard Edam-type "heart cheese" of Harmony™ and maintenance of normal blood pressure.

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BACKGROUND

Regulation (EC) No 1924/2006[4] 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 11/02/2014.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
- On 26/02/2014, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 27/03/2014, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 01/04/2014.
- On 06/05/2014, 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 14/05/2014 in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 27/05/2014, EFSA received the requested information and the clock was restarted.
- On 08/07/2014, 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 14/07/2014 in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 25/07/2014, EFSA received the requested information and the clock was restarted.
- During its meeting on 18/09/2014, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to "*Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type 'heart cheese' of Harmony™" and maintenance of normal blood pressure.

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: "*Lactobacillus plantarum*

[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.

TENSIA® in the semi-hard Edam-type 'heart cheese' of Harmony™" and maintenance of normal blood pressure.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of *Lactobacillus plantarum* TENSIA® a positive assessment of its safety, nor a decision on whether *Lactobacillus plantarum* TENSIA® 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: E-piim production Ltd. Pikk 16, Järva-Jaani, 73301, Järvamaa. Estonia.

Food/constituent as stated by the applicant

According to the applicant, the food and constituent for which a health claim is made is the semi-hard Edam-type Südamejuust (English translation: Heart cheese) of Harmony™ brand comprising probiotic strain *Lactobacillus plantarum* TENSIA®.

Health relationship as claimed by the applicant

According to the applicant, the claimed effect is maintenance of cardio-vascular health through reduction of blood pressure.

Wording of the health claim as proposed by the applicant

According to the applicant, regular, at least for eight week consumption of 50 g/day *Lactobacillus plantarum* TENSIA® comprising Südamejuust (English translation: Heart cheese) of the Harmony™ brand helps to maintain the cardio-vascular system/heart health through reduction of blood pressure/Symbol of heart/.

Specific conditions of use as proposed by the applicant

According to the applicant, the minimal amounts of 5×10^7 viable microbial cells in 1 g of cheese should be present per 50 g daily intake (i.e. the daily dose of the *Lactobacillus plantarum* strain TENSIA® consumed with this amount of cheese is 2.5×10^9 CFU). This quantity of cheese could be consumed as a part of a balanced diet.

The target population proposed by the applicant is the general population.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is *Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type "heart cheese" of Harmony™.

The bacterial strain *L. plantarum* TENSIA® has been isolated from a faecal sample of a healthy one-year-old Estonian child (Mikelsaar et al., 2002).

The strain *L. plantarum* TENSIA® (DSM 21380) species identity as well as strain characterisation have been determined by using phenotypic (carbohydrate fermentation profiles (API 50 CHL), enzymatic activities profile (API ZYM) and short chain fatty acid profile (gas chromatography)) and genotypic (Internal Transcribed Spacer-Polymerase Chain Reaction (ITS-PCR), 16S rRNA gene sequencing and sequence analyses, and agarose gel electrophoresis image after Random Amplification of Polymorphic DNA by PCR (RAPD-PCR)) methods. Data on the conditions of use, specifications, manufacturing process and bioavailability as well as information on the stability of the strain *L. plantarum* TENSIA® in freeze-dried powder are provided in the application.

The deposit of the strain at the German culture collection DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen) under deposit number DSM 21380 is indicated in the application.

The strain is used in the manufacturing process of a soft Edam-type cheese where the *L. plantarum* strain TENSIA® (10^6 CFU/mL cheese milk) is used as adjunct starter. Detailed specifications of the manufacturing process, stability information (survival and viable stability of the strain), characteristics and composition of the cheese were provided by the applicant.

The Panel considers that the food constituent *L. plantarum* TENSIA®, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is "maintenance of cardio-vascular health through reduction of blood pressure". The target population proposed by the applicant is the general population.

In the context of the scope of the application, which was submitted pursuant to Article 13(5) of the Regulation (EC) No 1924/2006, the Panel notes that the claimed effect relates to the maintenance of normal blood pressure.

Blood pressure (BP) is the pressure (force per unit area) exerted by circulating blood on the walls of blood vessels. Elevated blood pressure, by convention above 140 mmHg (systolic) and/or 90 mmHg (diastolic), may compromise normal arterial and cardiac function.

The Panel considers that the maintenance of normal blood pressure is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in MEDLINE, PubMed and esp@cenet. Keywords included "blood pressure lowering, nitric oxide, polyamines, cardiovascular health, *Lactobacillus plantarum*, CVD and probiotics, lactobacilli, milk peptides, ACE inhibitors". The search was limited to publications in English, Russian, and Estonian that were original research articles (peer-reviewed), reviews, consensus documents from 2000 onwards, or patent documents describing a relationship between lactobacilli, including *L. plantarum*, and blood pressure lowering and cardio-vascular health. The Panel notes that the literature search included terms such as *L. plantarum* and lactobacilli, but not *L. plantarum* TENSIA® (DSM 21380) in particular.

The applicant provided 47 (27 human and 20 non-human) references as being pertinent to the claim. These included four human intervention studies which investigated the effect of strains other than *L. plantarum* TENSIA® on blood pressure (Hata et al., 1996; Inoue et al., 2003; Seppo et al., 2003; Aihara et al., 2005), as well as guidelines, narrative reviews and *in vitro* studies which did not address the effects of *L. plantarum* TENSIA®. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

Two human intervention studies investigated the effect of the strain *L. plantarum* TENSIA® on blood pressure (BP) (Mikelsaar et al., 2012, 2013).

The unpublished study by Mikelsaar et al. (2013) is a randomised, double-blind, placebo-controlled parallel intervention which investigated the effects of consuming 50 g/day of Edam-type cheese containing *L. plantarum* TENSIA® (average daily dose of *L. plantarum* TENSIA® = 2.5×10^9 CFU) compared with the same amount of cheese without *L. plantarum* TENSIA® on BP in volunteers aged 18 to 65 years with high normal BP (systolic blood pressure (SBP) = 130-139 mmHg; diastolic blood

pressure (DBP) = 85-89 mmHg) or grade 1 hypertension (SBP = 140-159 mmHg; DBP = 90-99 mmHg) (ESC/ESH, 2013). Participants with SBP ≤ 129 mmHg or ≥ 160 mmHg and/or DBP ≤ 84 mmHg or ≥ 100 mmHg, as well as those who performed "extensive exercise" were excluded. The test and control cheeses, which were consumed daily for eight weeks, were distributed to participants at randomisation and at week 4. BP was measured at baseline, week 4 and week 8 by a nurse in one clinic centre. The study was conducted in two different time periods of the year (period I April–June 2012 and period II October–December 2012) owing to the difficulty in recruiting a sufficient number of subjects. Upon a request by EFSA for clarification on whether seasonal variations in BP may have affected the results of the study, the applicant indicated that randomisation was carried out in the two periods and that no influence was observed on SBP per treatment group and time period, and thus the period of randomisation was not taken into account in the statistical analysis.

The primary outcome of the study was the long-term (eight weeks) change in SBP. Secondary outcomes were long-term changes in DBP, and short-term (one to four weeks and five to eight weeks) changes in SBP and DBP. Total cholesterol, low-density lipoprotein-cholesterol, triglycerides, body mass index and waist-hip ratio, among others, were assessed as explanatory outcomes. A *t*-test was used for the analysis of the primary outcome, and the Wilcoxon rank sum test was used for the analyses of the remaining outcomes. The Panel notes that no scientifically sound reason was provided by the applicant to justify this choice.

A total of 136 participants who fulfilled the inclusion criteria at screening (visit 0) were randomised to consume the cheese with or without *L. plantarum* TENSIA® (n = 68 per group). Randomisation was stratified by age and sex. The Panel notes that, among the 136 participants randomised (intention to treat (ITT) population), 35 did not fulfil the inclusion/exclusion criteria at baseline (visit 1). The "modified" ITT (mITT) population was defined as all randomised participants with at least one primary variable measurement after baseline and no major protocol violations (n = 113, 57 and 56 in the test and control groups, respectively). The per protocol (PP) population was defined as all randomised participants meeting the inclusion/exclusion criteria at baseline who had valid endpoint measurements in addition to baseline and no major protocol violations. Upon a request by EFSA for clarification on the number of participants in each study group with complete data sets and who complied with the study protocol as planned, the applicant indicated that 60 participants (n = 32 in the test group and n = 28 in the control group) had complete data sets for BP measurements. Upon a request by EFSA for clarification on the compliance in the study, the applicant indicated that compliance with the study products was assessed using a questionnaire and quantitative PCR analysis of stools, which were collected in both study groups but analysed in only the test group.

Between-group differences in SBP and DBP changes throughout the study were analysed for the mITT population. SBP and DBP measured at baseline and at weeks 4 and 8 were not statistically different between groups. SBP significantly decreased in the test group (by 6.66 mmHg) compared with the control group (by 2.56 mmHg; p = 0.007) from baseline to week 8. Upon a request by EFSA for clarification, the applicant stated that a significant difference for the primary outcome was also observed using a non-parametric test (Wilcoxon test: p = 0.008). DBP significantly decreased in the test group (by 4.34 mmHg) compared with the control group (by 1.21 mmHg; p = 0.026) from baseline to week 8. SBP and DBP did not change significantly between baseline and week 4 in the test group compared with the control, whereas DBP (but not SBP) significantly decreased between weeks 4 and 8 in the test group (by 2.84 mmHg) compared with the control group (+0.24 mmHg; p = 0.002). Upon a request by EFSA for clarification on the reason for not using the ITT population for data analyses, the applicant stated that the use of the mITT population was preferred as important violations occurred in the ITT population, owing to the use of antibiotics and missing information at weeks 4 and 8.

Upon a request by EFSA, the applicant provided a sensitivity analysis using the ITT and PP populations for changes in SBP and DBP during the study. In the ITT population, SBP decreased by 6.81 mmHg in the test group and by 2.52 mmHg in the control group (p = 0.004), and, in the PP

population SBP decreased by 7.76 mmHg in the test group and by 3.31 mmHg in the control group (p = 0.021). The Panel notes that this analysis for the ITT population was based on 120 participants, and not on the 136 randomised participants. Data were also analysed by a mixed model using the mixed procedure in SAS and selecting an unstructured covariance structure. In the ITT population a statistically significant treatment by time interaction was observed for SBP (p = 0.025) with a difference in change from baseline to week 8 between groups of −3.86 mmHg (standard error (SE) = 1.44 mmHg; p = 0.008), whereas no statistically significant effect of treatment over time was observed in the PP population (p = 0.082). In the ITT population, a statistically significant treatment by time interaction was observed for DBP (p = 0.005), with a difference in change from baseline to week 8 between groups of –3.02 mmHg (SE = 1.22 mmHg; p = 0.015), whereas no statistically significant effect of treatment over time was observed in the PP population (p = 0.080).

The Panel notes that the different results obtained in the ITT, mITT and PP populations using the statistical analyses above can be explained by the low proportion of randomised participants who completed the protocol as planned in relation to the primary outcome (60 out of 136, 44 %), and this is an important limitation of the study, together with the fact that 35 of the randomised participants did not meet the inclusion criteria at baseline. The Panel considers that this study with important methodological limitations shows a blood pressure-lowering effect of *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ when consumed daily for eight weeks.

The intervention study by Mikelsaar et al. (2012) had already been submitted in a previous application for the same claim as an unpublished study report (referred to as Mikelsaar et al. 2009b). The claim was assessed by the Panel with an unfavourable outcome (EFSA NDA Panel, 2011). Briefly, this randomised, double-blind, placebo-controlled, cross-over human intervention study investigated the effects of consuming 50 g/day of Edam-type cheese containing *L. plantarum* TENSIA® compared with the same amount of cheese without *L. plantarum* TENSIA® on BP in healthy volunteers aged 18 to 65 years. The test and control cheeses were consumed daily for three weeks each with a washout period of two weeks in between. A total of 90 participants were randomised and 83 participants completed the trial. Changes in SBP and DBP were the primary outcomes of the study. No significant differences in SBP or DBP changes were observed between the intervention and control groups during the study. The Panel notes that this study does not show an effect of *L. plantarum* TENSIA® in Edam-type cheese on BP when consumed for three weeks.

Mechanism of action

The applicant indicated that the mechanisms by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert an effect on BP are probably complex and mainly related to the ability of the strain to produce metabolites (i.e. acetylcholine (Ach), angiotensin-converting enzyme (ACE) inhibitory peptides, nitric oxide (NO)) with vasodilation activity. The applicant provided three unpublished *in vitro* studies and a patent to support the proposed mechanisms for the claimed effect (Kilk, 2012; Mahlapuu and Rätsep, 2012; Songisepp et al. 2012; Ehrlich and Kilk, 2013).

The study by Mahlapuu and Rätsep (2012), reported significantly higher ACE-inhibitory activity of cow's milk fermented with *L. plantarum* TENSIA® than of control milk. The study by Ehrlich and Kilk (2013) investigated the ACE-inhibitory activity, and the concentration of some peptides, γ-aminobutyric acid (GABA) and Ach in a Südamejuust Harmony™ cheese prepared with *L. plantarum* TENSIA® as adjunct starter in a freeze-dried or liquid form compared with regular Edam-type cheese after one and four months of ripening. This study reported no statistical difference in the ACE-inhibitory activity between the test and control cheeses. Concentrations of other substances with a presumed vascular activity (i.e. the peptides isoleucine–proline–proline (Ile-Pro-Pro), valine–proline–proline (Val–Pro–Pro), phenylalanine–leucine (Phe–Leu), isoleucine–leucine (Ile-Leu), Ach, and GABA) in the intervention and control cheeses after one and four months of ripening did not follow a clear pattern. The study by Kilk (2012) reported a high concentration of

Ach in Südamejuust Harmony™ cheese with *L. plantarum* TENSIA® compared with Edam-type control cheese. No significant difference was observed in the concentration of the tripeptides Ile–Pro–Pro and Val–Pro–Pro between the test and control cheese, whereas a higher amount of Ile–Leu, Phe–Leu and isoleucine–proline–tyrosine was detected in the control cheese than in the test cheese. The applicant acknowledged that the biological significance of the peptides detected in the *L. plantarum* TENSIA® cheese has not been identified. Information on the *in vitro* production of NO and polyamines such as putrescine and N8-acetylspermidine by the strain *L. plantarum* TENSIA® was available in the patent provided by the applicant (Songisepp et al. 2012).

The Panel notes that no evidence was provided by the applicant for a mechanism by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert the claimed effect.

Weighing of the evidence

In weighing the evidence, the Panel took into account that only one human intervention study with important methodological limitations showed a BP-lowering effect of *L. plantarum* TENSIA® consumed in the Edam-type "heart cheese" of Harmony™ when consumed daily for eight weeks, and that no evidence was provided for a mechanism by which *L. plantarum* TENSIA® in the Edam-type "heart cheese" of Harmony™ could exert the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of *Lactobacillus plantarum* TENSIA®in the semi-hard Edam-type "heart cheese" of Harmony™ and maintenance of normal blood pressure.

CONCLUSIONS

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

- The food constituent *Lactobacillus plantarum* TENSIA®, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is "maintenance of cardio-vascular health through reduction of blood pressure". The target population proposed by the applicant is the general population. Maintenance of normal blood pressure is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of *Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type "heart cheese" of Harmony™ and maintenance of normal blood pressure.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on "*Lactobacillus plantarum* TENSIA® in the semi-hard Edam-type 'heart cheese' of Harmony™" and maintenance of normal blood pressure pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0411_EE). February 2014. Submitted by E-piim production Ltd.

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ABBREVIATIONS

ACE	angiotensin converting enzyme
Ach	acetylcholine
BP	blood pressure
CFU	colony-forming unit
DBP	diastolic blood pressure
GABA	γ-aminobutyric acid
Ile-Leu	isoleucine–leucine
Ile-Pro-Pro	isoleucine–proline–proline
ITT	intention to treat
NO	nitric oxide
Phe–Leu	phenylalanine–leucine
PP	per protocol
SBP	systolic blood pressure
SE	standard error
Val–Pro–Pro	valine–proline–proline