

## ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

## SARDINE PEPTIDE PRODUCT

**Issue**

Members are asked whether the applicant company's response to their earlier comments and objections to the marketing of Sardine peptide product as a novel food ingredient provide the necessary reassurance that the product meets the necessary criteria for authorisation as a novel food ingredient.

**Background**

1. Sardine peptide product (SPP) is a purified mixture of peptides (no peptide has a molecular weight greater than 870 Da). SPP is produced by enzyme catalysed hydrolysis of sardine muscle followed by chromatographic separation. The applicant intends to incorporate SPP into a range of conventional foods including dairy products, soups, stews and beverages as a functional food ingredient in order to control blood pressure. The applicant states that one particular dipeptide constituent (valine-tyrosine) of SPP is effective in the control of blood pressure.
2. On 10 March 2009, the European Commission forwarded to Member States the Finnish Competent Authority (CA)'s initial opinion on the application, which had been submitted by Senmi Ekisu Co. Ltd. made under Article 4(1) of Regulation (EC) No 258/97, for the authorisation of SPP as a novel food ingredient.
3. The Committee considered the application and the Finnish initial opinion at the April 2009 meeting (ACNFP/93/2). Members were unable to agree with the positive opinion of the Finnish CA and concluded that additional information is required before the assessment of the safety of the NI can be concluded. Members raised a number of comments and objections which formed the basis of the UK response to this application (**Appendix A**). These related to:
  4. **Animal Feeding Study:** Members expressed concerns relating to the absence of a 90 day feeding study, particularly as marginal side effects were observed in the 28 day study which should have been followed up with a 90 day study. This concern provided the basis for the UK's unfavourable response to this application.
  5. **ACE<sup>1</sup> inhibitory activity of SPP and potential interference with ACE-inhibitory medication:** Members were concerned about the potential of SPP to

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<sup>1</sup> ACE: angiotensin converting enzyme

interfere with medication that may be taken by hypertensive individuals e.g. ACE inhibitors. Members also highlighted the possibility that hypertensive individuals may consume SPP in favour of prescribed medication.

6. **Post-market monitoring:** Members expressed that given SPP is on the Japanese Market, it would have been valuable if the applicant had provided post-market monitoring data.
7. As noted in the previous paper ACNFP/93/2, the Secretariat approached the Medicines and Healthcare Regulatory Agency (MHRA) for advice on the blood pressure-related health claims made by the applicant for SPP and the apparent ACE-inhibitory activity of SPP,. The MHRA advised that SPP would probably be considered medicinal in the UK.

### **Applicant's response**

8. The applicant's responses to the Committee's concerns are summarised below and the full response is attached as **Appendix B**.
9. Five other Member States also commented on the Finnish initial opinion. The applicant's response to all Member States' concerns is attached at **Appendix C (restricted)**.

### **(i) Animal Feeding Study**

Appendix B p.3-4.

10. The applicant considers that further long term studies are not justified because the marginal effects observed in the 28 day study were not of toxicological significance and no statistically significant or dose dependent changes were observed in the majority of toxicological parameters assessed. The applicant highlights that the only statistically significant change observed was a marginal increase in male left kidney weights in the high dose group but no gross lesions were observed and there was no difference in histopathological findings between control and high dose males.

### **(ii) ACE inhibitory activity of SPP and potential interference with ACE-inhibitory medication**

Appendix B p.1-2, 4-5

11. The applicant states that, although valine-tyrosine appears to compete for the same transport mechanism as the ACE inhibitor captopril, SPP-containing foods are unlikely to interfere with the absorption of captopril if it is taken as directed.

The applicant's reasoning for this is that captopril is intended to be taken one hour before meals to ensure effective absorption.

12. The applicant further explains that SPP-containing foods would not pose a risk to individuals taking antihypertensive medication because only a minimal percentage of valine-tyrosine is absorbed following intake of SPP (0.014% of valine-tyrosine is absorbed in humans following intake of 12 mg of valine-tyrosine). The applicant reiterates that the intake of peptides from Senmi's ingredient is estimated to be considerably lower than the background dietary intake of proteins (including sardine protein from existing sources).
13. The applicant's view is that although valine-tyrosine has been manufactured to exert a physiological effect, it has low bioactivity which is limited to homeostatic maintenance of healthy blood pressure and is therefore not a drug intended for use in the management of hypertension. The applicant states that, although valine-tyrosine may share a similar mechanism of action with pharmacologically active ACE inhibitors such as captopril, the observed activity is far lower. The applicant highlights that other dietary peptides derived from enzyme-treated proteins of various food origins have also been shown to have similar properties and are natural to the human diet.

### **(iii) Post-market monitoring**

Appendix B p.5-6

14. The applicant has provided information relating to sales of SPP in tablets, tea and drinks in Japan between 2001 and 2009 and states that no adverse effects were reported during this time period.

### **Committee Action Sought**

15. The Committee is asked whether the applicant's responses are sufficient to adequately address their earlier comments and objections.
16. Members are also asked whether there are any other issues that they wish to comment on arising from the applicant's response to points raised by other Member States.
17. The Committee's comments will be used to inform the Agency's position in future discussions regarding this novel ingredient at meetings of the Standing Committee on the Food Chain and Animal Health.

**Secretariat  
September 2009**

**Appendices attached:**

Appendix A: Letter to the Commission with the ACNFP's comments on the Finnish  
Competent Authority's Initial opinion

Appendix B: Applicant's response to the UK's comments

Appendix C: (restricted) Applicant's response to all Member States' comments

**Appendix A to ACNFP/94/7**

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Letter to the Commission with the ACNFP's comments on the Finnish Competent Authority's Initial opinion.

**Secretariat  
August 2009**



**Appendix B to ACNFP/94/7**

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Applicant's response to the UK's comments

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**ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES**

Other Member States comments on the Finnish Competent Authority's initial opinion  
**(RESTRICTED)**

**Secretariat  
September 2009**