

**ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES**

**LUCERNE LEAF EXTRACTS**

**Issue**

The Committee is asked to consider an initial opinion from the French Competent Authority on an application for authorisation of a protein, mineral and vitamin complex and a protein ingredient obtained from lucerne leaves for use respectively as a food supplement and food ingredient under the Novel Foods Regulation (EC) No. 258/97.

The Committee is asked whether it agrees with the initial opinion and whether they have any further comments to make on the application. The Committee's advice will form the basis for the UK's formal response.

**Introduction**

1. On 27 February 2003, the European Commission forwarded the French Competent Authority's (CA) initial opinion on an application made under Article 4(1) of Regulation (EC) No 258/97 from a French company, Viridis. Under the time scales set out in the regulation, the UK and other Member States have until 26 April 2004 to provide comments or objections to the initial opinion.
2. The French CA has sought advice from their food safety agency, AFSSA, and has issued a negative opinion for this novel food.
3. A translation of the French Initial Assessment Report and the full dossier from the applicant, including supplied references, are attached as Annexes 1 and 2 respectively.

**Background**

4. Pursuant to Regulation (EC) No 258/97, the application from Viridis is for placing on the market of the two following products obtained from the fractionation of leaf proteins from the same lucerne biomass (*Medicago sativa* L.):
  - (i) A complex of proteins , minerals and vitamins - PROLIVI
  - (ii) A protein ingredient - RUBISCO
5. The proteins, minerals and vitamins (PMV) complex will be marketed in Europe as a food supplement. It has been given to children from developing countries, since 1992, in order to overcome their dietary deficiencies. The protein ingredient is intended to be sold to food manufacturers as a food ingredient for its functional

emulsifying and foaming properties, but could also be used in the formulation of dietary supplements.

6. In accordance with the European Commission Regulation 258/97, the PMV complex and the protein ingredient obtained from lucerne leaves have been classified under article 1 paragraph 2 part (e) as a food or food ingredient isolated from animals. Using the Commission guidelines for the safety assessment of novel foods (97/618/EC), these products have been classed as a complex novel food from a non-GM source (class 2.2). The requirements for a submission for this class are as follows:

**The key issues for consideration are presented below under the stated headings taken from the European Commission guidelines on scientific information necessary to support applications for placing on the market of novel foods or novel food ingredients.**

### **I Specification of the Novel Food (NF)**

(Annex 1 page 6)

7. Leaves of the lucerne plant *Medicago sativa* L. are used by Viridis for the production of a PMV complex and a protein ingredient. The composition of these two protein ingredients is as follows:
  - (i) PMV complex: 35-55% proteins, minerals (Ca, Fe, Mg) and vitamins A, D, E and K.
  - (ii) Protein ingredient: 80-90% non-chloroplast proteins which are mainly enzymatic (ribulose 1-5 diphosphate carboxylase/oxygenase)

### **II Effect of the production process applied to the NF**

(Annex 1, appendix 1 p. A1-1&2)

8. The two extracts are obtained from the same lucerne biomass which is crushed and pressed to obtain a green juice. This juice is submitted routinely to colorimetric and microbiological analysis. Further to its filtration, the juice undergoes six successive processing stages<sup>1</sup> to finally obtain a PMV complex and a protein ingredient. The PMV complex is heated at 90°C, concentrated and dried at 105°C which destroys bacterial flora and heat-sensitive anti-nutritional substances. The protein ingredient is obtained through acid precipitation, filtration and pasteurisation before being dried at a maximum of 60°C.
9. The French CA was satisfied with the production process involving high-performance separation technologies which have been tested in an EU research programme. Viridis is certified to ISO 9002 and carries out control analysis of samples taken at different production stages. The quality of the finished products complies with the recommendations made by the GEPV<sup>2</sup>.

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<sup>1</sup> (1) thermocoagulation of proteins at 85-90°C, (2) clarification, (3) fractionation, (4) microfiltration, (5) pasteurisation, (5) spray-drying.

<sup>2</sup> Groupe d'Experts en Photovoltaïque (Study Group on Plant Proteins)

### **III History of the organism used as the source of the NF**

(Annex 1, p. 7 & 9)

10. In Europe, lucerne has been used in the forms of dry biomass and protein meals, for at least the past 50 years, to feed farm animals. The nutritive value of dried lucerne has been improved by developing a dried lucerne concentrate which contains high levels of proteins and xanthophyll, which is used for its pigment content by the animal feed industry.
11. Populations of both North & South Americas and China have been consuming leaf extracts from lucerne or alfalfa for their nutritional and dietary benefits, the main advantage being to prevent infantile malnutrition.

### **IX Anticipated intake and extent of use of the NF**

(Annex 1 p. 7 & 8, Appendix 2)

12. The French CA was content with the nutritional property of PMV complex which is intended to promote children's growth and correct anaemia. The applicant recommends an intake of:
  - 5 g/day for children weighing less than 15kg,
  - 10 g/day for children weighing from 15 kg to 40 kg and
  - 15 g/day for adolescents and adults weighing more than 40 kg.

Viridis mentioned that some people might not digest this extract easily when eaten for the first time, therefore, it recommended that the doses be administered in increments of 2.5g/day. Viridis did not give any information on the intended use of the PMV complex in the EU in order to justify the need of this food supplement at the proposed level for European children.

13. The protein ingredient will be used for its emulsifying and foaming properties and could replace ingredients such as soya concentrate or egg proteins in various foods, at an incorporation level of 3 to 7%. Additionally, the table in Appendix 2 of Annex 1 shows the similarities in protein, carotene and xanthophyll contents of 100g of a foodstuff containing the protein ingredient at the recommended level with 250g of spinach. The French CA noted that the applicant did not specify whether this ingredient would be used exclusively as a food ingredient. If this ingredient is also to be used for its high protein content in the formulation of dietary supplements (5-10% level), the French CA concludes that the applicant must ensure that the nutritional properties are generally satisfactory where it is to be used as the main source of protein.

### **XI Nutritional information on the Novel Food**

(Annex 1 p. 9-15 tables 1 - 5, appendix 3 )

14. Details of the amino acids, lipids, carbohydrates, vitamins and minerals levels found in PMV complex are given in pages 9 to 13 of Annex 1 (Tables 2 to 5). The table in Appendix 3 of Annex 1 shows the respective percentages of the Recommended Nutritional Intake (2001) for children, adolescents and adults for proteins, vitamin A, iron and calcium contained in PMV complex. No major remark was made by the French CA on this.
15. The French CA noted that the amino acid composition of protein ingredient is well-balanced (table 1 p. 9 of Annex 1) and that its nutritive value was excellent and generally higher than most protein foods.

## **XII Microbiological Information**

(Annex 1 p.14, table 6)

16. The French CA was satisfied with the microbiological safety of the two lucerne extracts and pointed out that the applicant has implemented a robust quality control system at different stages of its production line.

## **XIII Toxicological information**

(Annex 1 p. 14-18 table 7, appendix 4)

17. The two leaf extracts do not have levels of pesticide residues, mycotoxins and heavy metals which exceed the GEPV's reference values and the current recommendations made by the CHPCF<sup>3</sup>. The levels of inherent anti-nutritional compounds (total polyphenols) are also acceptable for both extracts. More specifically, the levels of saponins are below the levels found in peas, soya or lentils which are commonly eaten in Europe.
18. It has been reported that consuming lucerne sprouts and seeds can trigger a risk of a systematic lupus erythematosus (SLE)-type autoimmune reactions in humans. This has been attributed to the presence of L-canavanine in lucerne leaves, although the role of other substances has not been ruled out. The applicant has argued that L-canavanine was present at low levels in both extracts and, furthermore, could be destroyed by the heat-treatment applied to the PMV complex and the purification process applied to the protein ingredient. Moreover, the data given in appendix 4 of Annex 1 shows that lentils have a much higher level of L-canavanine than lucerne. However, the French CA felt that current knowledge is insufficient to rule out the potential risk of the two extracts causing SLE- type autoimmune reactions in consumers with this syndrome.
19. The potential allergenicity of the leaf extracts of lucerne was only assessed in animals. It was understood that the lack of data from human studies was partly due to the fact that lucerne is not consumed in Europe. Therefore, the French CA suggested that Viridis should provide further data showing the cross-reactivity between protein of the extracts and allergens of leguminous plants known to be allergenic (e.g. ground nuts).
20. Although the studies on malnourished children show the nutritional benefits of the protein extracts, they are not supportive of the intended use of these extracts in Europe. The French CA would have preferred to see results from a study on healthy individuals with no nutritional deficiencies (e.g. risk of excessive vitamin intake). It was also noted that the applicant did not carry out any reproductive toxicity study or no-effect dose study to determine the acceptable daily intake of the lucerne extracts.
21. The French CA concluded that insufficient toxicological and allergenicity analyses were carried out to demonstrate the safety of the two lucerne extracts.

## **Committee Action Sought**

22. The initial assessment report from the French CA concludes that further assessment is required before these two extracts can be authorised for use as novel food ingredients, in order to address the following issues:

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<sup>3</sup> Conseil Supérieur d'Hygiène Publique de France (French Public Hygiene Advisory Committee)

- incomplete nutritional information (paragraph 13)
- incomplete toxicological data (para 18)
- information on potential cross-reactivity with existing allergens (para 19)

23. The French CA has also questioned the need for PMV complex in the EU population (para 20).

24. Members are asked whether they agree with the French CA's conclusions and whether they have any further objections, or comments on this application.

**Secretariat**  
**March 2004**