Safety Assessment of Vitamin K_2 (MenaQ7 pure and MenaQ7 advanced products) as a novel food

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Novel Food Classification: 1.2. (f)

Introduction

An application for the authorisation of a synthetic vitamin K_2 (MenaQ7 Pure and MenaQ7 advanced products) was submitted to the Food Safety Authority of Ireland (FSAI) by NattoPharma ASA of Norway in accordance with *Article 4* of the novel food Regulation (EC) No. 258/97. The application was accepted by the FSAI on May 29th, 2014.

The novel ingredient is a synthetic vitamin K_2 similar to that placed on the market by Kappa Biocience AS following a novel food application which was assessed by the German authorities and granted access to the EU market in 2012.

The applicant intends to market the novel ingredient in the same food groups and at the same levels as vitamin K_2 sources already on the market. A 2008 EFSA opinion addressed the safety and bioavailability of a biologically derived vitamin K_2 added for nutritional purposes to foods for particular nutritional uses and foods (including food supplements) intended for the general population.

This synthetic vitamin K_2 is classed by the applicant as novel in accordance with *Article 1.2(f)* of the novel food Regulation (EC) No 259/97; "Foods and food ingredients to which has been applied a production process not currently used, where that process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism or level of undesirable substances". The application dossier was prepared pursuant to Commission Recommendation 97/618/EC and in order to assess wholesomeness, the novel ingredient was considered in Class 6: "Foods produced using a novel process".

I. Specification of the novel food

The applicant provides comprehensive data detailing the physical, chemical and structural identity of the novel ingredient. The synthetic vitamin K_2 product is a light yellow crystalline or oil form of high purity (> 99%) and comprises menaquinone 7 predominantly. It is light sensitive and insoluble in water but soluble in a number of organic solvents. The stability of the novel ingredient was demonstrated under ambient and accelerated conditions for up to 6 months, with further studies ongoing.

II. Effect of the production process applied to the novel food

The NattoPharma vitamin K_2 is manufactured at a production plant in the pharmaceutical research institute in Warsaw to GMP standards. Considerable details of the production and purification processes are provided which are considered by the

applicant as standard in the production of fat-soluble vitamins and which utilise menadione, isoprene and trans, trans-farnesol as the initial substrates. The synthetic product is packaged in 1 kg or 5 kg aluminum bags with recommended storage at ≤ 25 °C while protected from light.

The final vitamin K_2 product is of very high purity, confirmed by batch test results. The applicant maintains that potential contaminants include post-synthetic residues such as residual starting materials, side products and degradation products which are present at insignificant levels and therefore not of concern. The applicant also addresses possible residues such as heavy metals (including residues from catalysts) as well as solvent residues with no concerns being identified.

III. History of the organism used as the source of the novel food

This section is not applicable as the NattoPharma MenaQ7 is a synthetic product.

IX. Anticipated intake/extent of use of the novel food

The addition of vitamin K_2 (biologically derived and synthetic) as a source of vitamin K is already permitted for certain foodstuffs in the EU. Supplementation with vitamin K_2 in these food categories is regulated under distinct legislative instruments and includes dietetic foods (Regulation (EC) No 953/2009), food supplements (Regulation (EC) No 2000/46) and general foods (Regulation (EC) No 1925/2006) and take into account the Scientific Committee for Food (SCF) opinion of 2003 on The Tolerable Upper Intake Level of Vitamin K. An EFSA opinion in 2008 addressed the safety of and bioavailability of vitamin K_2 as a source of vitamin K when added to various foodstuffs. The NattoPharma vitamin K_2 will provide an alternative source of the vitamin along with other commercial sources and will adhere to existing use and recommended intake levels.

X. Information from previous human exposure to the novel food or its source

Vitamin K_1 (phylloquinone) and vitamin K_2 (menaquinone) occur naturally and humans have a long history of dietary exposure to these fat soluble vitamins. The safety of vitamin K_2 intake as a source of vitamin K has been assessed by the NDA panel of EFSA in an opinion published in 2008, while intake levels of vitamin K were addressed in an opinion of the SCF in 2003 (republished by EFSA in 2006). The safety of a synthetic vitamin K_2 was addressed in a novel food application by Kappa Bioscience and which was granted access to the EU market in 2012.

XI. Nutritional information on the novel food

The applicant provides information about the natural and exogenous sources of vitamin K_2 which itself has no calorific value but plays a coenzyme role in certain biochemical processes. The EFSA opinion on a novel food application for biologically derived vitamin K_2 along with the SCF opinion deals extensively with the nutritional and other aspects of vitamin K_2.

XII. Microbiological information on the novel food

The microbiological status of the novel ingredient was not addressed extensively in this application as it is unlikely that any microbial growth or survival will be supported during the production of this synthetic vitamin K_2. The applicant notes that the use of ethanol in the final step of the synthesis will make the survival of any microbial contaminant very difficult.

XIII. Toxicological information on the novel food

Extensive toxicological information relating to vitamin K_2 is publically available and has been assessed previously by EFSA and more recently as part of the authorisation of another synthetic vitamin K_2 as a novel food ingredient to Kappa Bioscience AS. For this reason, no new toxicological data is provided in this application and the applicant instead discusses the existing information provided in the form of references to the literature and previous opinions expressed by EFSA on the safety and bioavailability of vitamin K_2. The only volatile solvents detected in the final product were ethanol and ethyl acetate. Both of these solvents are considered to be of low toxicological potential and were detected at less than 10% of guide limits.

Conclusions

The applicant has carried out extensive analysis to demonstrate that their novel ingredient is vitamin K_2, predominantly all-trans Menaquinone 7. The applicant demonstrates that any side-products resulting from the multi-step synthesis are reduced to an insignificant level by the built-in purification steps, leaving a final product of high purity. The potential for residual solvents or heavy metals is addressed and no concerns identified. Because the novel ingredient is chemically identical to its biologically derived counterpart as well as that produced by a different synthetic process, it can be assumed that the positive conclusions of safety assessments already carried out on those forms of vitamin K_2 would also apply in this case. The only potential differences that could arise would include possible contaminants arising from the production process and the applicant has addressed these aspects satisfactorily. Intended uses for the novel vitamin K_2 are identical to existing comparators and are already governed by current legislation including its use in dietetic foods (Regulation (EC) No 953/2009), food supplements (Regulation (EC) No 2000/46) and general foods (Regulation (EC) No 1925/2006).

Recommendation

The Food Safety Authority of Ireland has not identified any safety concerns associated with the placing on the market of synthetic vitamin K2 (MenaQ7 pure and MenaQ7 advanced products) by NattoPharma ASA and therefore considers that it meets the criteria for novel food set out in *Article 3.1.* of the novel food Regulation (EC) No 258/97.