Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

Evaluation of an application to use Fullerene C_{60} as a food additive

Opinion of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety

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Contributors

Persons working for VKM, either as appointed members of the Committee or as *ad hoc* experts, do this by virtue of their scientific expertise, not as representatives for their employers. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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Contents

Background

The Norwegian Food Safety Authority (Mattilsynet) has asked the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) to conduct an evaluation of the use of Fullerene C_{60} as a food additive based on the provided documentation from an applicant. The case has been assessed by the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics.

The applicant has applied for a permission to use Fullerene C_{60} as an admixture/antioxidant in salmon- and fish oil and claims improved storage stability of fish oil in the presence of this preservative. The current application was submitted to the Norwegian Food Safety Authority 30.06.2008. An application of the same product for the same use was submitted by the company 29.06.2006. This first application underwent a preliminary evaluation by this VKM Panel, which concluded that the application could not be assessed due to lack of data and poor presentation.

The VKM Panel has now evaluated if the new application fulfils "Guidance on Submissions for Food Additive Evaluations by the Scientific Committee on Food, SCF, European Commission, 11 July 2001" which is used by the European Food Safety Authority in such evaluations (SCF, 2001). The European Food Safety Authority (EFSA) has later (09.07.2009) adopted a new scientific opinion on the data requirements for the evaluation of food additives (EFSA, 2009), but since the application was submitted prior to this, it will be evaluated with regard to the prior guidance document.

The application is submitted as a dossier with headings in line with the preferred format outlined in the guidance document. The dossier has referred to 63 reports, articles and patents. None of these were made available for the VKM Panel.

Terms of reference

The Norwegian Food Safety Authority requests the Norwegian Scientific Committee for Food Safety (VKM) to consider if the documentation in the updated dossier from the applicant is in accordance with SCF's guidance on submissions for food additive evaluations, and if sufficient data now have been included, for the application to be submitted to the EU Commission and EFSA for further evaluation.

Assessment

General comments

The compound in question is, no doubt, a molecule of high scientific and industrial interest. However, the VKM Panel would like to express concern of using this as a preservative food additive, since it according to the applicant seems to have multiple biological and medical effects. It is, according to the dossier, claimed to exhibit antiviral and antimicrobial effects, it prevents cold and it can be used as a beautifying cosmetic ingredient. Generally, a technical food additive like a preservative should clearly exhibit this effect, but be biologically inert in other circumstances.

The substance applied for and to be documented is the Fullerene C_{60}. Derivatives of this, which are made water-soluble by attaching hydrophilic side groups or carrying peptide/protein side chains can provide supportive information, but must be regarded as another substances. This is so, because the derivatisation will have impact on the absorption, distribution, metabolism and elimination of the compound, as well as on any mechanism of toxicity. If the application seeks approval also for the derivatives, specific data for each of these must be submitted.

Fullerene C_{60} is of particle nature (nanoparticle). Nanoparticles are suspected to have special properties with regard to absorption, distribution and accumulation in the organism and consequently there are additional safety aspects. In a full evaluation of the use of Fullerene C_{60} as a food additive, these aspects have to be included. The dossier has to address these concerns.

In the following, major deficiencies and relevance of the submitted data are commented upon according to the headings of the dossier.

Summary document

A literature review of other uses of Fullerene C_{60} and similar compounds are given, but information on intended use is scarce. Further comments are given under the specific parts.

Part I Administrative data

Regarding the manufacturer of the substance it seems odd that this is produced by a professor at an analytical centre connected to the Russian Academy of Science. Is this a manufacturing company responsible for the quality of the production? This should be further explained.

Part II Technical data

1. Identity of substance

The VKM Panel understands that the substance applied for is Fullerene C_{60}. Specifications should be confirmed by analytical data of typical production batches.

2-3. Microbiological characteristics

Microbial specifications should be given and compliance shown by analytical data.

4. Manufacturing process

The extraction and purification procedure is not well described. The VKM Panel would like to question why extraction from salmon oil is part of the manufacturing process. Critical information is quality of raw material, typical batch size, yield, chemicals and solutes used in the extraction and purification, analysis of raw material, intermediates and finished product. The flow chart is unclear.

5. Method of analysis in food

It is not clear if the methods for analysis in food (UV and NMR) are qualitative or quantitative. Limits of detection and quantification, and precision should be given together with examples of actual analytical data.

6. Reaction and fate in food

This important section has not been answered. The mechanism of action and a characterisation of the reaction products resulting from the anticipated oxidation of Fullerene C_{60} are considered necessary information.

7. Case of need and proposed uses

The topic is reasonably addressed. The antioxidative effect of Fullerene C60, compared with Vitamin E, seems convincing.

8. Exposure

Data from biopharmaceutical and cosmetic use of Fullerene C_{60} derivatives are of limited relevance. Figures for human exposure of the preservative have not been given.

Part III Toxicological data

This part is poorly presented and it is difficult to understand which substance has been tested, in what doses and which study design used. Two "acute toxicity studies" are referred, one in mice with 70 days observation and one in rats with 91 days observation, both with macroscopic pathology. The VKM Panel has the opinion that this design is unusual and does not comply with any testing guidelines (OECD or other). Studies are necessary for all toxicological endpoints required (SCF, 2001). These studies should be properly designed according to an accepted guideline and comply with Good Laboratory Practice (GLP). Data on the water-soluble derivatives of Fullerene C_{60} can be supportive for the evaluation, but can never replace safety data on the substance applied for. It is anticipated that the toxicokinetic properties and also the toxicity of Fullerene C_{60} and its water-soluble derivatives could be quite different.

Conclusion

The dossier is poorly presented and the summarised data are difficult to understand. Most of the key safety data are lacking and the relevance of some of the summarised data are questioned. It can be stated that the application cannot be assessed due to absence of crucial data. The VKM Panel is of the opinion that the application does not fulfil the requirements for being evaluated by the EU Commission and EFSA.

Documentation provided to VKM

Technical dossier 2008. Application about recognition of Fullerene C_{60} as an admixture/antioxidant used as stabilization in salmon- and fish oil. June 2008. Submitted by UNI Pharma Holding AS, Halsa, Norway.

References

EFSA (European Food Safety Authority) (2009) Scientific Statement of the Panel on Food Additives and Nutrient Sources added to Food on data requirements for the evaluation of food additives applications following a request from the European Commission. *The EFSA Journal* (2009) 1188, 1-7.

SCF (Scientific Committee on Food) (2001) Guidance on submissions for food additive evaluations by the Scientific Committee on Food (opinion expressed on 11 July 2001), European Commission, Health & Consumer Protection, Directorate-General. SCF/CS/ADD/GEN/26 Final 12 July 2001.