Meeting

Olive Fruit Dry Extract Discussion Paper

Committee Paper for Discussion - ACNFP/162/05

Advisory Committee for Novel Foods and Processes

Application for Authorisation as a Novel Food for Olive Fruit Dry Extract Standardized in Hydroxytyrosol

Application number RP1074

Issue

The Committee reviewed this application for the first time at the April 2023 meeting where members requested further information. The Committee is invited to consider the response from the applicant and whether it addresses the request for clarification satisfactorily or if further information is required.

Background

1. In April 2021, the FSA received the submission for olive fruit dry extract standardized in hydroxytyrosol, a food supplement ingredient. The novel food ingredient is an extract of *Olea europea* L. fruit, standardized to either 10% or 20% hydroxytyrosol. The applicant intends to use the novel food as an ingredient in food supplements for those over 18 years of age, excluding pregnant and breastfeeding women.

2. The applicant explains the novel food status has been determined by the Spanish authorities following a consultation process. As such it would be considered not to have a history of consumption in the UK and EU. They also note that pure hydroxytyrosol is authorised in dietary supplements in France and Italy, and hydroxytyrosol obtained by chemical synthesis has been authorised in fish and vegetable oils in the UK.

3. The Committee reviewed this dossier for the first time on 26th April 2023 where further information was sought from the applicant in the following areas: production process, composition and specification, stability, proposed used levels and anticipated intake, and allergenicity.

4. The Committee is asked whether the applicant's response addresses the outstanding questions from their request for information. To inform the discussion, the FSA requested further information (Annex A) and the applicant's response (Annex B) are provided. All other supporting data is in Annex C.

Applicant's response to request for further information

Production Process

5. The members noted that a column based purification process was used. Further information was requested on the column, the basis for its purification, the potential for leachates, the controls on cleaning and if reused. The applicant states that the basis for hydroxytyrosol purification is the physical adsorption of hydroxytyrosol on the adsorbent resin. They outline the column process in detailed steps (Annex B) with the aid of flow diagrams. This includes information on how many times the column is used before being replaced and controls on the process.

6. Further information was sought on how the elution from the column is monitored including the elution profile. The applicant explains hydroxytyrosol concentration and total dry matter (total olive juice compounds) are monitored in all leachates and that hydroxytyrosol and other phenolic compounds are analyzed by HPLCDAD and total dry matter is determined by gravimetry. They also refer back to the provided representative batches of the products (10 and 20% hydroxytyrosol).

Composition and Specification

7. The Committee noted that the proximate analysis that had been provided was on the novel ingredient plus the carrier. The Applicant has presented Annex 24 and 25 (Annex C) providing the nutritional values for both extracts before the addition of carrier and excipients. A summary table has been provided (Annex B). They explain that the main difference between the two fractions is the

concentration in phenolic compounds, which is lower in the fraction used to obtain the 10% extract and is counterbalanced by a higher content in carbohydrates.

8. Further information was sought on the function of the carrier and excipients in order to understand the properties of the final extract. The applicant states that the main purpose of the carrier and excipients are related to technological issues. They explain that the product without carrier and excipient is liquid, and therefore, less convenient for use in food supplements, which normally are in solid form. The use of carrier and excipient aims in obtaining a powder instead of a liquid, which does not affect the safety and other characteristics of the final ingredient.

9. Members noted that no information had been provided on the mass on drying and therefore the contribution of water was unclear. In response, the applicant explains that the aqueous fraction that concentrates the hydroxytyrosol is concentrated (by reduced pressure evaporation) and dried (by spray drying) to obtain a final product in powder form with a very low moisture content (5%). Humidity, measured by gravimetry, has been provided for 3 samples of the 10% extract and 3 additional samples from the 20% extract. Results showed a slightly lower humidity in the 10% extract (2.75 to 2.84%) compared to the 20% extract (3.37 to 3.87%). However, the applicant suggests this slight difference does not affect the characteristics of the ingredient.

10. The applicant was also requested to provide more information on the total polyphenols present in the extract. They provided the average values measured by HPLC and expressed as hydroxytyrosol. For the 10% extract, average hydroxytyrosol was 10.3%, 4.4% average other polyphenols and 14.7% average total polyphenols. For the 20% extract, the values were 20.2%, 8.6% and 28.8% respectively.

Stability

11. The members noted that from the from the information provided the focus in the stability study appeared to be the hydroxytyrosol. The applicant was asked to explain whether any other compounds – such as breakdown products from other constituents in the extract, carrier or excipient were tested and the reason for their decisions.

12. The applicant explained that the HPLC assays performed during the stability study showed no additional peaks, suggesting the lack of breakdown product and

that the stability test results also showed the lack of change in hydroxytyrosol and tyrosol concentrations in the product. Hydroxytyrosol was used in stability studies as it represents the main polyphenol of the product.

Proposed Use and Intake

13. It was noted that breastfeeding women had been excluded from the proposed users but other vulnerable groups such as infants and children were included. The applicant was asked to explain the reasoning for excluding this group. The applicant explained that section 2.7.2 of the dossier highlighted exclusion of children below 18 years of age as well as the other vulnerable groups. They further explain that exclusion is due to the lack of adequate safety data in these vulnerable groups.

Absorption, Distribution, Metabolism and Excretion (ADME)

14. The members noted that a range of data using different materials had been presented to support the ADME and Toxicological review. It was requested that this information be summarised to allow the relevance of the data to be understood. The applicant has provided this in Annex B.

15. Further information was also sought on the Margin of Safety calculation.. The applicant has provided detailed explanation (Annex B) concluding the definition of the safe dose of the extract is based on the following information the fact that olive fruit is consumed worldwide, without any significant safety concern and that hydroxytyrosol is safe, as recognized by EFSA in their review of the application.

16. They further explain that the proposed daily intake of the novel food is based on the available sub-chronic toxicity studies, which provide a margin of safety greater than the 200-factor that is considered the standard safety factors to apply when moving between studies in rats to humans. They noted that with the exception of one study which showed no side effect of an olive fruit extract with a low concentration of hydroxytyrosol, limiting the conclusion that can be drawn from this study regarding the safety of hydroxytyrosol.

Allergenicity

17. As covered under composition further information was requested on the proximate analysis of the extract and in particular the protein content. The applicant states that Annexes 24 and 25 (Annex C) show that the protein content of the aqueous fraction is 1.13 and 0.12% for the fractions used to obtain the 10% and 20% extracts respectively. This low level, the applicant suggests would minimise the risk of allergic responses in those sensitised to Olives.

18. Further information was sought on the source of the starch used as a carrier in the formulation and whether it contained known allergens. The applicant has provided more information on the starch in Annexes 26 and 27 (Annex C). They explain that the maltodextrin is obtained from maize and is therefore devoid of gluten as indicated in the documents provided by the supplier Annex 28 (Annex C).

Committee Action Required

- The Committee is asked whether the response from the applicant is sufficient to clarify the concerns discussed at the last meeting.
- If not, the Committee is asked to indicate what further data is required and the feedback that should be given to the applicant.

ACNFP Secretariat

July 2023

Annexes (Confidential)

Annex A – Request for further information

Annex B – Applicants response

Annex C – Supporting documents