Meeting

Vitamin D2 Mushroom Powder Discussion Paper

Committee Paper for Discussion - ACNFP/162/07

Advisory Committee for Novel Foods and Processes

Application for Authorisation of Vitamin D2 Mushroom Powder Discussion Paper as a Novel Food.

Application number RP1550

Issue

An application has been received under the novel food authorisation process (regulation 2015/2283 as retained in UK law) for vitamin D2 mushroom powder.
The Committee is asked to advice on whether the available data provides an adequate basis for a risk assessment, and whether the novel food is safe and not nutritionally disadvantageous under the proposed use and use levels.

Background

1. In April 2022, the FSA received the submission for vitamin D2 mushroom powder from Monterey Mushrooms, LLC. The novel food consists of *Agaricus bisporus* mushrooms that have been exposed to UV light to catalyse the conversion of endogenous ergosterol within the mushrooms to vitamin D2, then ground to a powder.

2. Treatment of foods with UV light is a novel process and while a number of UV treated foods including mushrooms have been authorised as these are subject to slightly different processes each has been subject to review and authorisation separately..

3. The applicant proposes the use of the novel food at levels of 2.25µg/100g for food products, 1.12ş µg/100ml for beverages and food supplements at 15µg/day for a population of over 1 year of age and 10µg/day for infants 7-11 months.

4. The application dossier is attached as Annex A, the annexes to the dossier attached as Annex B. Annex C contains the EFSA opinion on the safety of vitamin D2 mushroom powder. All annexes contain confidential information.

This Application Identification

5. The identity of this novel food is verified by high performance thin layer chromatography with the full report in Annex I (Annex B). The chemical name, CAS number, trade name, structure and scientific name have been provided. The applicant requests that the identity details of this novel food be kept confidential.

Production Process

6. The applicant has provided both confidential and non-confidential details of the production process. The only raw material used in production of vitamin D2 mushroom powder is *A. bisporus* mushrooms which are grown and harvested in the US under controlled environmental conditions in compliance with Regulation (EC) No. 852/2004 and within the principles of HACCP (Annex B: Annex I).

7. Once the mushrooms are received from the farm, they are isolated by organic or conventional status, where they are then sliced or diced to increase the surface area for exposure before being placed onto a variable speed conveyor which is covered with UV light units adjusted according to the targeted level of vitamin D2 and the exposure times. Once dry, they are placed on plastic trays and stacked.

8. They are then dehydrated and ground before being transferred to plastic bags that are sealed. Prior to packaging, composite samples are taken from the batch and sent for microbial analysis and analysis of vitamin D2 content. When necessary, batches of powder are blended proportionately to create new batches that achieve the targeted vitamin D level. A detailed description of the production process is provided (Annex A: section B) including a flow diagram.

Composition

9. The applicant has provided analytical data for five independent representative batches concluding that their analysis indicates that their product consistently

meets the proposed specifications for the novel food. All the Certificates of Analysis and methods are provided in Annex II (Annex B). They report that the analysis of vitamin D2 is conducted using a proprietary method, validated for use with vitamin D2 mushroom powder. Vitamin D2 is assayed using high-performance liquid chromatography with a synthetic vitamin D as an internal standard.

10. The applicant has reported heavy metal analysis for arsenic, cadmium, mercury and lead from 6 independent batches detailed in table 2.c.1.2.1-1 (Annex A). They further explain that the maximum levels detailed in the table were taken from the closest relevant categories detailed in Commission Regulation (EC) No 1881/2006 as amended. They conclude that the results demonstrate that the levels of heavy metals are consistent within the proposed product specifications and well below established EU limits.

11. The presence of aflatoxins were measured in 6 independent batches of vitamin D2 mushroom powder with the results are presented in Table 2.c.1.2.2-1 (Annex A). The maximum levels were taken from the closest relevant category (cereals and all products derived from cereals, including processed cereal products) detailed in Commission Regulation (EC) No 1881/2006, as amended, for aflatoxin B1 and the total sum of B1, B2, G1 and G2. They conclude the results demonstrate that the levels of aflatoxins are consistently low, within proposed product specifications and established EU limits.

12. The applicant stated that a multi-residue pesticide screen was conducted on a representative batch of vitamin D2 mushroom powder (Batch Number B2018 317 A05-VAR) using Pesticide Analytical Manual VOL. I, Section 302-E1, and that no pesticides were detected in vitamin D2 mushroom powder.

13. The applicant conducted microbial analysis of the novel food on 5 independent batches presented in Table 2.c.1.2.4-1 and 2.c.1.2.4-2, with the conclusion that the results illustrate that microbiological contaminants are all below specification limits.

14. They also investigated by analysis three batches for the presence of biologically inactive photoisomers (lumisterol and tachysterol) which are formed during the conversion of ergosterol to vitamin D2. These photoisomers are also formed endogenously in humans during cutaneous production of vitamin D following exposure to UV-B radiation from sunlight. The results are presented in Table 2.c.1.3-1 (Annex A) and they conclude that these results demonstrate that only negligible amounts are detected in the final ingredient.

Stability

15. The applicant stated that the intended shelf life of this product is 3 years. They conducted 3 year tests on 4 batches and 4 year test on 1 batch. They concluded that the results as presented in Table 2.c.3.1-1 (Annex A) supported the proposed 3 year shelf life. They also carried out microbial stability tests for 3 years with results shown in Table 2.c.3.2-1 (Annex A) suggesting that that the product is stable for up to 3 years under recommended storage conditions (as described in section 2.c.3.1 (Annex A)). Full report can be found in Annex III (Annex B).

16. They also performed similar testing on stability of vitamin D2 content within vitamin D2 mushroom powder on some foods that the novel food would be an added ingredient (fruit juice drink and cereal bar), as well as any sensory changes. They conclude that for both finished products, there were little changes in taste and vitamin D2 content. Full report can be found in Annex III (Annex B) and Annex A p22-26.

Specification

17. The applicant has provided specification Table 2.d-1(Annex A p27) of the novel food. They also state that 12̲5̲ to 462.5̲µg/g of vitamin D2 content is considered to be the minimum concentration of vitamin D2 within the powder required to allow for small enough quantities to be used to meet the requirements for a “source” of vitamin D2, without affecting the organoleptic properties of the foods and beverages to which it will be added.

History of Use

18. The applicant states that wild edible fungi, including cultivated and wild grown *A. bisporus* mushrooms (source of the novel food) have been consumed within and outside of the UK for a long time. UV-treated *A. bisporus* mushrooms have also been consumed in the UK with their approval as a novel food ingredient since 2016.

19. The novel food, Monterey’s vitamin D2 mushroom powder has no history of use in the UK. However, a similar ingredient, vitamin D2 mushroom powder (produced by homogenisation of mushrooms before exposure to UV light, as opposed to vitamin D2 mushroom powder, where the mushrooms are first exposed to UV before being dried and ground into a powder) was authorised as a

novel food in 2020. Another form of vitamin D2 mushroom powder was considered safe under its intended uses by EFSA in 2021 (Annex C).

20. The applicant performed a literature search to identify literature related to the safety of vitamin D2, vitamin D2 mushroom powder, or other related UV-exposed mushroom products, published since February 2021, when EFSA adopted their opinion on the safety of vitamin D2 mushroom powder (*Agaricus bisporus*) as a novel food. These studies are discussed in section 2.i (Annex A) under toxicology.

Proposed Use and Intake

21. The applicant states the target population for this novel food is the general population excluding infants under 7 months of age.

22. The proposed maximum use levels of the novel food are 2.25µg/100g (15% of the AI) for food products, 1.125µg/100ml (7.5% of the AI) for beverages, food supplement at 15µg/day for food supplements for age +1yr and 10µg/day for food supplements for infants 7-11 months, which is intended to provide the full AI for vitamin D for the relevant age groups. This is based on EFSAs recent defined adequate intake (15µg/day) as a replacement for nutrient reference value.

23. A summary of the foods proposed to use the novel food as an ingredient and the use levels for the powder is provided in Table 2.f.2-1 (Annex A). Some of these include breakfast cereals, dairy analogues, fruits and vegetable juices and nonalcoholic beverages.

24. Estimates for the total daily intakes of vitamin D2 and the novel food itself from all proposed conventional food uses in the UK are provided in Sections 2.f.3.1 and 2.f.3.2, respectively (Annex A).

25. A summary of the estimated daily per kilogram body weight intake of vitamin D2 from vitamin D2 mushroom powder from food supplements is provided in Table 2.f.4.1-1. The maximum intended use level in foods for special medical purposes is 15µg vitamin D2/day, excluding those intended for infants. This is with the assumption that the powder would be the only source of vitamin D in the diet. This is also the same maximum amount intended for total diet replacement for weight control and meal replacements for weight control.

26. The applicant states that approximately 17g of fresh mushrooms are used to produce 1g of vitamin D2 mushroom powder. This therefore means that even the highest estimated intakes of vitamin D2 mushroom powder (121.4 mg/day for

male adults) equates to consumption of only 2.1 g of fresh mushrooms. With an average serving of mushroom being approximately 70g, they estimate the intake of fresh mushrooms from worst-case consumption of vitamin D2 mushroom powder is negligible, in comparison to a serving of mushrooms.

27. Combined intake from the novel food and other sources is discussed with estimated daily intake of vitamin D from the total diet presented in Table 2.f.6-1 (Annex A). This calculates the cumulative exposure of vitamin D from the total diet. The applicant concludes that based on these results, 29µg/day for infants up to and including 11 months of age, and 2ʂ and 26.3µg/day for toddlers and other children, respectively, do not exceed the UL of 3ʂµg/day established by EFSA for infants aged 6 to 12 months of age and that of ʂ0µg/day for children aged 1 to 9 years. Similarly, the cumulative intakes of vitamin D from the total diet of 19.9, 30.ʂ, and 23.3µg/day among adolescents, adults, and elderly subjects, respectively, are well below the UL of 100µg/day for each of these population groups.

Absorption, distribution, metabolism and excretion

28. The applicant undertook 2 studies using UV-Irradiated mushroom products supplied by Monterey. The first human ADME study, a randomised, doubleblinded, placebo-controlled 6-week study involving 38 healthy adults (14 males and 24 females) (Annex A: p39), it was concluded that that vitamin D2 from UVexposed mushrooms is absorbed and metabolized to 25(OH)D2, and consumption did not affect overall vitamin D status because of the proportional decrease in serum 25(OH)D3.

29. The second human ADME study, a 12-week randomised study where 25 healthy adults consumed either UV-exposed mushroom extract (supplied by Monterey), vitamin D2 supplement or vitamin D3 supplement (all providing ʂ0µg vitamin D2/day) in capsules once daily for 12 weeks. The study concluded that the mushroom extract was as effective at increasing and maintaining total serum 25(OH)D levels as supplemental vitamin D.

Nutritional information

30. Section 2.h in the dossier (Annex A) discusses the nutritional information including a brief literature review in conjunction with the composition section

which provides the proximate analysis in Table 2.c.1.1-1 and nutritional analysis of five independent batches in Table 2.c.1.2-1 (Annex A p16). Justification of the proposed use levels is discussed. The applicant states that novel food is not nutritionally disadvantageous under the proposed conditions of use and that the nutritional content of mushrooms exposed to UV light is unchanged, with the exception of the intended increase in vitamin D2 content.

31. The applicant states that Vitamin D2 from UV-irradiated mushrooms has been shown to be bioavailable in several human studies using 25(OH)D as an indicator (Annex A: Section 2.i.6) and that increases in 25(OH)D have also been observed in animal studies. Dose-related increases in 25(OH)D were observed in samples from rats that had consumed bread prepared with UV-treated baker's yeast in which vitamin D2 is formed from endogenous ergosterol in an analogous way to that seen in UV-treated mushrooms.

Toxicological information

32. In support of this application, the applicant has highlighted authorised foods that are UV treated; UV-treated baker's yeast, UV-treated bread, UV-treated milk.

33. They also highlight EFSA recently concluded a similar product was safe; vitamin D2 mushroom powder (produced by homogenisation of mushrooms before exposure to UV light), under the proposed conditions of use for the proposed target populations in absence of any ingredient-specific toxicological studies hence, this should retrospectively discern safety issues for this novel food and that no toxicology studies should be deemed acceptable, with the source (mushrooms) having a long history of use.

34. For the sake of completeness of this application, the applicant has completed short term and subchronic toxicity studies on similar UV-exposed mushroom products, with a summary provided in Table 2.i.3-1 (Annex A p44-46) with no safety issues raised. These studies further support the safety of vitamin D2 mushroom powder.

35. The applicant explored literature review on human studies with a discussion provided in Annex A p49-54 giving the conclusion that daily consumption of UVB-exposed *A. bisporus* mushrooms providing up to 65̨µg (2,600 IU) vitamin D2/day for 16 weeks was not associated with any reported adverse effects and that Vitamin D2 from UV-B-exposed *A. bisporus* mushroom products was demonstrated to be bioavailable in all studies, as evidenced by increased serum

25(OH)D2 (the direct metabolite of vitamin D2) concentrations. Summary Table 2.i.6.3-1 on human studies has been provided (Annex A: p53-54).

Allergenicity

36. The applicant has considered the allergenicity potential of the novel food and concluded that novel food has no known allergenic concerns either as mushrooms or after UV treatment.

Committee Action Required

- The Committee is asked whether the available data provide a satisfactory basis for evaluating the safety of this novel food ingredient?
- If so, the Committee is asked whether it is content to recommend approval of the novel food as an ingredient to be added to the range of foods specified?
- If not, the Committee is asked to indicate what additional data would be required?

ACNFP Secretariat

July 2023

Annexes

Annex A - Dossier

Annex B - Annexes to the Dossier

Annex C - EFSA Opinion