Meeting

Calcidiol Discussion Committee Paper for Discussion

Committee Paper for Discussion - ACNFP/153/08

Advisory Committee For Novel Foods and Processes

Application for Authorisation of Calcidiol as a Novel Food.

Additional Information from applicant – Application number RP35

Issue

The Committee reviewed this application for the first time at the June 2021 meeting and for the second time at the November 2021 meeting where they requested further information so as to proceed with their assessment. Members are invited to consider the response from the applicant and assess whether it addresses the requests for information satisfactorily or if further information is required.

Background

1. On the 12th of January 2021, the FSA (Food Standards Agency) received the submission for “Calcidiol” from DSM Nutritional Products Ltd (Switzerland). Calcidiol is a new form of Vitamin D for use as a food supplement targeted at a generally healthy population including pregnant and lactating women, except children under 3 years. It is a vitamer of vitamin D3 (cholecalciferol) and is directly absorbed by the human body.

2. During the review in the November meeting, the Committee raised several areas where further information was required to assess the safety of the novel food and its proposed use. Information was requested in the following areas:

- Identity
- Production process
- Proposed use and intake
- Toxicological information

The Secretariat requested further information in Annex A which is included with the applicant’s response in Annex B and associated appendices Annex C (contains confidential information).

Applicants’ response to request for further information Identity

3. Further reassurance was sought on whether Calcidiol was structurally the same as the metabolite in the vitamin D metabolite. The data given did not provide enough clarity with further information being requested. The applicant responded by providing Chapter 3 of the Ullmann’s Encyclopaedia of industry Chemistry (Annex C) to support their argument that the method they have used is standard for the compound as outlined in their response (Annex B). Further to that, they refer back to specifications (file “05_1_Specifications and “04_1_Compositional Updated 210420”) to confirm Calcidiols’ identity. Additionally, a Certificate of Analysis has been submitted to prove presence of Calcidiol in the product (Annex C – COA HD3).

Production Process

4. The Committee advised the applicant to provide a comprehensive HACCP plan that included the steps in the production process, any risks introduced, any risks mitigated and the steps taken to manage the identified risks. The applicant has responded with a more detailed HACCP plan that is to be treated as confidential (Annex C – HACCP). They have further pointed out in their response that key risks have been identified with their effective management in place as highlighted in their initial HACCP submission (initial HACCP - Annex C).

Proposed use and intake

5. In consideration to the applicants suggested use levels and that Calcidiol is 3 times as bioavailable as vitamin D, the Committee suggested that this should be considered as 5 times bioavailable so as to take into account of variation in responses and the need to be cautious on the impact of efficacy. The applicant

has responded explaining the scientific basis for their assertion that Calcidiol is 3 times more potent that vitamin D3. However, noting the preference for a conservative factor of 5 to account for the variation in the responses, this will be considered.

6. The Committee raised concerns on the impact of the greater bioavailability on the potential for risks at the suggested dosage especially due the margin between a recommended dose and the upper intake level considered safe being. The applicant was further asked to comment on the rationale as to why the dose proposed is safe for a UK population. The applicant clarifies that the proposed maximum reference intake level should not be related to a recommended daily intake but rather to the tolerable upper intake level (UL) of vitamin D as set by EFSA or IOM per age ranges. The applicant further supports the safety of the proposed intake levels by putting their toxicology study results in perspective with literature references documenting doses from which hypercalcemia occurs as detailed in their response in Annex B. They also reiterate that the recommended daily dose will be managed through labelling with clear warning not to exceed this dose.

Toxicology

7. The applicant was asked to reconsider the implications of differences in metabolism of vitamin D by women during pregnancy and lactation especially because there is literature evidencing that metabolism of vitamin D3 in these women is different. The applicant was asked whether they anticipate there are different risks from Calcidiol for this group. The applicant agrees that metabolism in pregnant women is changed especially with respect to hormonal levels. However, justify why they consider their recommended maximum dose to be safe for pregnant women by compounding the change in metabolism in pregnant women with an increased risk of deficiency in this population and the additional role of vitamin D in immune pathways during pregnancy. They further provide literature reference supporting an increase in serum 25OHD concentration in response to vitamin D supplementation being similar in pregnant and lactating women compared to non-pregnant or non-lactating women.

Committee Action Required

- The Committee is asked whether the response from the applicant is sufficient to complete the risk assessment.

- If not, the Committee is asked to indicate what additional information would be required.

Annexes (Confidential)

Annex A– Request for further information

Annex B – The applicants response

Annex C – Response Annexes