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Safety and efficacy of a feed additive consisting of 25-hydroxycholecalciferol produced with *Saccharomyces cerevisiae* CBS 146008 for pigs and poultry for the renewal of its authorisation (DSM Nutritional Products Sp. z.o.o)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the assessment of the application for renewal of authorisation of 25-hydroxycholecalciferol as a feed additive for pigs and poultry. The applicant provided data demonstrating that the additive currently in the market complies with the conditions of authorisation. The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concludes that the additive does not give raise to any safety concern regarding the production strain. Considering that the manufacturing process, the composition of the additive and its conditions of use have not been modified, the Panel considers that there is no evidence to reconsider the conclusions reached in the previous assessments. Therefore, the Panel concludes that 25-OH-D_3 remains safe for the target species, the consumer and the environment under the existing conditions of the authorisation. The additive is not irritant to the skin or eyes but no conclusion on its potential to be a skin sensitiser or on its effects on the respiratory system can be reached due to absence of data. There is no need to assess the efficacy of the additive in the context of the renewal of the authorisation.

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Keywords: nutritional additive, 25-hydroxycholecalciferol, vitamin D, pigs, poultry, safety, efficacy

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest 1 year before the expiry date of the authorisation.

The European Commission received a request from DSM Nutritional Products Ltd[2] for renewal of the authorisation of the product 25-hydroxycholecalciferol, when used as a feed additive pigs and poultry (category: nutritional additive; functional group: vitamins, pro-vitamins and chemically well-defined substances having similar effect).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 14(1) (renewal of the authorisation). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 2 April 2019.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product 25-hydroxycholecalciferol, when used under the proposed conditions of use (see Section 3.1.5).

1.2. Additional information

25-Hydroxycholecalciferol (25-OH-D_3, synonyms calcidiol or calcifediol) is a semi-synthetic product. [redacted].

EFSA published three opinions on the use of 25-OH-D_3 as a feed additive, one on the safety and efficacy for chickens for fattening, turkeys and laying hens (EFSA, 2005), one the safety and efficacy for poultry and pigs (EFSA, 2009) and one on the safety and efficacy for all pigs, all poultry for fattening and ornamental birds and other poultry species (EFSA FEEDAP Panel, 2023). The EFSA Panel on Nutrition, Novel Foods and Food Allergens (EFSA NDA Panel) has recently adopted an opinion on the safety of calcidiol as a novel food (EFSA NDA Panel, 2021).

25-OH-D_3 is currently authorised in a stabilised form for use in feed for chickens for fattening, turkeys for fattening, other poultry and pigs (3a670a).[3]

The European Pharmacopoeia (2023) has monograph 01/2019:1295 dedicated to calcifediol monohydrate (synonym of 25-hydroxycholecalciferol monohydrate).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier in support of the authorisation request for the use of 25-hydroxycholecalciferol as a feed additive. The dossier was received on 22/10/2018 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2019-00104.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' (elicitation) knowledge, to deliver the present output.

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

[2] DSM Nutritional Products Ltd, Wurmisweg 576, 4303 Kaiseraugst, Switzerland represented in the EU by DSM Nutritional Products Sp. z.o.o.

[3] Commission Regulation (EC) No 887/2009 concerning the authorisation of a stabilised form of 25-hydroxycholecalciferol as a feed additive for chickens for fattening, turkeys for fattening, other poultry and pigs.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of 25-hydroxycholecalciferol in animal feed.[4]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of 25-hydroxycholecalciferol is in line with the principles laid down in Regulation (EC) No 429/2008[5] and the relevant guidance documents: Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2021).

3. Assessment

25-Hydroxycholecalciferol (25-OH-D_3) is currently authorised as a nutritional feed additive (functional group: vitamins, pro-vitamins and chemically well-defined substances having similar effect) in feed for chickens for fattening, turkeys for fattening, other poultry and pigs. The applicant requested the renewal of the authorisation for the above species.

The additive is authorised as a stabilised form of the active substance 25-OH-D_3. The term 'additive' in this opinion will be used to refer to the stabilised form of 25-OH-D_3 as described by the applicant (see Section 3.1.4).

3.1. Characterisation

3.1.1. Characterisation of the production strain

The precursor of 25-OH-D_3, 5,7,24-cholestatrienol, is produced by fermentation with a genetically modified strain of *Saccharomyces cerevisiae* which has been deposited with the Westerdijk Fungal Biodiversity Institute under the accession number CBS 146008.[6] The taxonomic classification of the production strain was confirmed [redacted].[7]

3.1.2. Information relating to the genetically modified microorganism

Characteristics of the recipient or parental microorganism

The production strain CBS 146008 was derived from the parental strain [redacted] The production strain under assessment shares the parental [redacted] with the strain ATC 1562 that was the production strain that formed the basis for the former opinions (EFSA, 2005, 2009).

Description of the genetic modification process

[redacted]

[4] Evaluation report received on 17 September 2020 and available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en.
[5] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.
[6] Technical dossier/Supplementary information December 2019/Appendix 13.
[7] Technical dossier/Section II/Annex II.10.
[8] Technical dossier/Section II/Annexes II.10, II.13 and II.15 and Supplementary information December 2019/Appendix 14

[redacted]

3.1.3. Characterisation of the active substance

The active substance 25-hydroxycholecalciferol ((3*S*,5*Z*,7*E*)-9,10-secocholesta-5,7,10(19)-triene-3,25-diol monohydrate; IUPAC name: (1*S*,3*Z*)-3-[(2*E*)-2-[(1*R*,3a*S*,7a*R*)-1-[(2R)-6-hydroxy-6-methyl heptan-2-yl]-7a-methyl-2,3,3a,5,6,7-hexahydro-1H-inden-4-ylidene]ethylidene]-4-methylidenecyclohex an-1-ol;hydrate; synonyms: calcidiol, calcifediol; 25-hydroxy vitamin D_3) is identified with the Chemical Abstracts Service (CAS) number 63283-36-3 and the European Inventory of Existing Chemical Substances (EINECS) number 621-370-5.[9] The molecular formula is $C_{27}H_{44}O_2 \cdot H_2O$ and its molecular weight is 418.66 Da. The structural formula is represented in Figure 1.

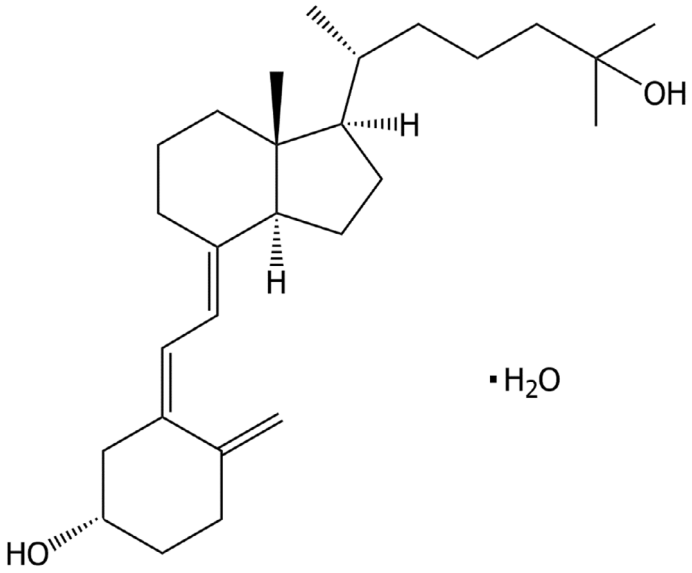

Figure 1: Structural formula of 25-hydroxycholecalciferol monohydrate

The authorisation by Commission Regulation (EC) No 887/2009 followed the previous specification and characterises the active substance with 25-hydroxycholecalciferol > 94%, other related sterols < 1% each and erythrosine < 5 mg/kg. The applicant is proposing to keep the same specifications with regards the minimum content of the active substance and the limit for erythrosine, but to change the specifications for other related sterols from '< 1% each' to '≤ 1% each'. The applicant justifies this change with the fact that the values measured by the analytical method are whole numbers, either 0 or 1. The applicant also set specifications for water ≤ 5% and for the sum of other sterols ≤ 6%.

The applicant stated that no changes have been introduced in the manufacturing or composition of the product (except for a change in the antioxidant used in the additive, see Section 3.1.4).

[9] Technical dossiers/Section II.

Data on the batch to batch variation of five recent batches of the active substance showed compliance with the above specifications.[10] Analytical data on batch-to-batch variation (five batches analysed) showed average concentrations of 25-OH-D_3 of 104% (range 103–105%), other related sterols ranged 0–1% and erythrosine was below the limit of detection (LOD: 0.08 mg/kg).[11] Water was 4% in all five batches and the sum of other sterols averaged 1.3% (range 0.9–1.7%).

25-OH-D_3 is insoluble in water, soluble in acetone, ethanol, DMSO and other lipophilic solvents. Its melting point is 100–120°C.

Apart from erythrosine and the other sterols, the applicant set specifications for aluminium and lead (≤ 20 mg/kg) and for total organic solvents used in the manufacturing process (≤ 1%). Data from five batches showed compliance with the specifications.[12]

The presence of viable cells [redacted][13][redacted]. No viable cells were detected.

The presence of recombinant DNA of the production strain [redacted][14][redacted] The analyses showed no amplification in any of the samples from the three batches (while positive PCR control gave amplification). [redacted].

3.1.4. Characterisation of the additive

Since 25-OH-D_3 is sensitive to light, heat and oxidation, the authorisation foresees that it is placed in the market as a stabilised form of the active substance. The applicant provided information of a stabilised form of 25-OH-D_3 (ROVIMIX® Hy•D® 1.25%), which was already described in the previous opinion on the same additive (EFSA, 2009). The product is an 'off-white to yellowish' fine powder that contains 25-OH-D_3 at 1.25%. It also contains 25 g sodium ascorbate, 50 g vegetable oil, 715 g modified food starch, 150 g maltodextrin and 10 g silicon dioxide[15] (E 551) per kg of additive. The applicant proposed to change the original antioxidant (ethoxyquin) with butylated hydroxytoluene (BHT), 37.5 g/kg. Apart from this, the applicant confirmed that no other modifications or changes in the manufacturing or composition have been introduced since the original authorisation.

Five recent batches of ROVIMIX® Hy•D® 1.25% were examined for the content of the active substance.[16] The average content of 25-OH-D_3 was 1.34% (range 1.31–1.37%) and a loss on drying of 2.8% (range 2–3%).

3.1.4.1. Impurities

Levels of lead, cadmium, mercury and arsenic analysed in three batches of the additive were below the respective limit of quantification (LOQ).[17]

The same three batches were also analysed for aflatoxins and dioxins. The aflatoxins B1, B2, G1 and G2 were all and in all samples below 0.5 μg/kg. Polychlorinated dibenzo-*p*-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) were analysed in three batches where most of the congeners were not detected. Exceptions were one heptafuran congener (234678-HpCDF 0.0506 ng/kg) and an octa digoxin (OCDD 0.205 ng/kg) in one batch; and a hexafuran congener (123789-HxCDF 0.103 ng/kg) in another batch. The calculated upper bound, expressed as World Health Organization (WHO) PCDD/F toxic equivalents (TEQ), for the three batches ranged 0.06–0.10 ng WHO-PCDD/F-TEF/kg.[18]

[10] Technical dossier/Section II/Annex_II_02.
[11] Technical dossier/Section II/Annex_II_16 Limit of Quantification for erythrosine: 2 mg/kg additive.
[12] Technical dossier/Section II/Annex_II_02 and Supplementary information November 2021.
[13] Technical dossier/Supplementary information April 2020/Appendix 16.
[14] Technical dossier/Supplementary information December 2019/Appendix 15.
[15] Currently under re-evaluation.
[16] Technical dossier/Section II/Annex_II_06_CoAs_HyD.
[17] Technical dossier/Supplementary information December 2019/Appendix 3. LOQ: lead, cadmium and mercury = 5 ng/g; arsenic = 10 ng/g.
[18] Technical dossier/Supplementary information December 2019/Appendix 2.

The values are all below the respective thresholds (Directive 2002/32/EC) and, when those thresholds cannot be identified, without safety concern.

Solvents used in the production of the 25-OH-D_3 include methanol, acetone, 2-propanol, ethyl isopropanol, tetrahydrofuran heptane and ethyl-acetate. Analysis of three batches showed values for methanol between 168 and 204 mg/kg, tetrahydrofuran was below the LOQ (720 mg/kg) and the other solvents < 10.0 mg/kg.[19] Compliance with the maximum levels for residual solvents used in veterinary drugs is provided (EMA, 2010).

3.1.4.2. Physico-chemical characteristics

Three lots of the additive were analysed for dusting potential using Heubach Test Type I equipment according to DIN55992-1 and the analytical values ranged 2,300–2,600 mg/m^3.[20]

Regarding the potential presence of nano-particles in 25-OH-D_3, the applicant submitted the same information as for the assessment as novel food (EFSA NDA Panel, 2021).[21] In the published opinion of NDA is indicated:

'The NF has a particulate nature and the morphology and number-based size distribution of the particles have been characterised by means of transmission electron microscopy-energy dispersive X-ray analysis (TEM-EDX), in accordance with the ISO norm 21363:2020, and scanning electron microscopy (SEM). The NF is a polydisperse material composed of small irregular particles with a median length, width and thickness of 541, 333 and 264 nm, respectively. The D10 of the length, width and thickness are 201, 144 and 108 nm, respectively The NF contains a fraction of nanoparticles (the minimum length, width and thickness being 111, 76 and 19 nm, respectively).

In addition, the Panel notes that the NF is composed of small particles and contains a fraction of nanoparticles (see Section 3.2), which are insoluble in water. The applicant provided an in vitro study simulating human gastrointestinal (GI) digestion, which showed that these particles do not quickly dissolve in the GI tract, implying that a fraction may reach the human intestine as particles. However, if the NF is absorbed at least partly as small particles or nanoparticles, they are expected to partition and quickly solubilise into the lipophilic compartments, suggesting that systemic distribution of particles is unlikely to occur.

Following absorption, the NF, if taken up as nanoparticles, is expected to partition and quickly solubilise into the lipophilic compartments, suggesting that systemic distribution of particles is unlikely to occur. Taking all this into account, the available toxicological studies are considered adequate for the assessment'.

The FEEDAP Panel agrees with the assessment of the NDA Panel.

3.1.4.3. Stability and homogeneity

New data were provided on the shelf-life of the additive.[22] Three batches of the additive were stored in standard packaging at 15, 25 or 40°C for up to 24, 18 or 6 months, respectively. Recoveries were at least 90% when stored at 25 or 40°C and above 95% when stored at 15°C. No additional data were submitted regarding the stability in premixtures or complete feed or on the homogeneity. The Panel considers that the data already assessed in the context of the previous opinion still apply to the current application (EFSA, 2009).

3.1.5. Conditions of use

25-OH-D_3 is currently authorised for use in feed for chickens for fattening and turkeys for fattening at a maximum use level of 0.100 mg/kg complete feed, in feed for other poultry at a maximum of 0.080 mg/kg complete feed and in feed for pigs at a maximum of 0.050 mg/kg complete feed.

Under the other provisions it is reported:

- The additive shall be incorporated in feedingstuffs via the use of a premixture.
- Maximum content of the combination of 25-hydroxycholecalciferol with vitamin D_3 (cholecalciferol) per kg of complete feedingstuff:
  - ≤ 0.125 mg (equivalent to 5,000 IU of vitamin D_3) for chickens for fattening and turkeys for fattening,

[19] Technical dossier/ Supplementary information December 2019/Appendix 1.
[20] Technical dossier/Supplementary information December 2019/Appendix 4 and Supplementary information November 2021.
[21] Technical dossier/supplementary information December 2022/Appendix_2 and Appendix_3.
[22] Technical dossier/Supplementary information December 2019/Appendix 5.

- ≤ 0.080 mg for other poultry,
- ≤ 0.050 mg for pigs.

- Simultaneous use of vitamin D_2 is not allowed.
- The content of ethoxyquin shall be indicated in the label.
- For safety: breathing protection shall be used.

The applicant proposes to maintain the same conditions of use.

3.2. Safety

The recipient strain from which the production organism was derived belongs to *S. cerevisiae*, which is considered by EFSA to be suitable for the qualified presumption of safety (QPS) approach to safety assessment when used for enzyme production (EFSA, 2007; EFSA BIOHAZ Panel, 2023). The genetic modifications performed to obtain the production strain CBS 146008 have the purpose to increase the production of trienol. As a result of the genetic modification, the production strain harbours an ampicillin resistance gene. However, viable cells of the production strain and its DNA were not detected in the additive. Therefore, the additive does not give raise to any safety concern regarding the genetically modified production strain.

The safety of 25-OH-D_3 for the target species, consumers, users and environment was assessed by the FEEDAP Panel in its previous opinions (EFSA, 2005, 2009). In the latest opinion (EFSA, 2009), the FEEDAP Panel concluded that the 25-OH-D_3 at the maximum inclusion levels of 0.100 mg/kg, 0.080 and 0.050 mg/kg was safe for chickens and turkeys for fattening, other poultry and pigs, respectively. The FEEDAP Panel also concluded that there were no concerns for the consumer safety and no risks for the environment were expected. In the same opinion it was concluded that the additive is not irritant to the skin or eyes. Data on skin sensitisation as well as on respiratory toxicity were not provided.

The applicant conducted a structured literature search in order to provide evidence that the additive remains safe under the approved conditions of use for target animal species, consumers, users/workers and the environment.[23] Several databases (ECHA, IPCS INCHEM, TOXNET, ScienceDirect, Google Scholar, PubMed and AGRIS) were searched for safety information. The search was limited to information available since 2009 to 2018. The main keywords were related to the active substance. Inclusion and exclusion criteria applied for the selection were provided. This database search was further updated and covered the period 2009–2019.[24]

The literature search resulted in 47 papers that were considered relevant for the assessment of the safety of 25-OH-D_3. Most of the papers dealt with the use of 25-OH-D_3 in pigs and poultry. Only one paper was identified which provided information relevant to the safety for the consumer. No relevant hits were identified with regards to the safety for the user or the environment.

Most of the studies in target animals assessed the effects of the inclusion of 25-OH-D_3 in the diet as a replacement of vitamin D_3 on performance parameters of poultry and pigs (including reproductive performance) when used at levels below or up to the maximum authorised level in the EU. Only one of the studies assessed the use of levels higher than the maximum authorised in pigs (von Rosenberg et al., 2016). The authors of this study evaluated the effect of a supplementing feed for weaned piglets with 25-OH-D_3 at 5 or 10 times the maximum authorised level for 42 days. Although this study showed several limitations (low number of replicates (2) per treatment, no statistical analysis of feed intake and feed to gain, limited parameters analysed for blood haematology and chemistry) which prevent an adequate assessment, no adverse effects of the supplementation with 25-OH-D_3 on the parameters assessed were reported.

Overall, none of the papers identified in the literature search reported a safety concern for the target species.

With regards to consumer safety, only one paper was identified which included data on the deposition of 25-OH-D_3 in tissues of pigs (Quintana et al., 2010). However, the Panel notes that this publication reported the same values/results which were already considered in the opinion of 2009 (EFSA FEEDAP Panel, 2009).

[23] Technical dossier/Section III/ Annex_III_02.
[24] Technical dossier/Supplementary information December 2019/Appendix 6.

3.2.1. Genotoxicity

The genotoxicity of 25-OH-D_3 was assessed by the FEEDAP Panel in 2005 and 2009 (EFSA, 2005, 2009). In the present assessment, the applicant submitted a series of new genotoxicity tests which were not available for the previous assessments.[25] These studies included an Ames test, an *in vitro* gene mammalian cell gene mutation in mouse lymphoma cells and an *in vivo* rat micronucleus test in bone marrow. These studies were assessed by the NDA Panel in the context of the application of 25-OH-D_3 monohydrate as a novel food (EFSA NDA Panel, 2021). The NDA Panel concluded that, on the basis of the studies assessed previously by the FEEDAP Panel and the newly submitted ones, there was no concern for genotoxicity for 25-OH-D_3. The FEEDAP Panel agrees with this assessment and this conclusion.

3.2.2. Reassessment of the consumer exposure

In its first opinion (EFSA, 2005), the FEEDAP Panel proposed a provisional upper tolerable limit (UL) for 25-OH-D_3 of 10 μg/day in adults and adolescents (11–17 years) and 5 μg/day in children (0–10 years). This was based on the UL for vitamin D_3 (50 μg/day in adults and 25 μg/day in children up to 11 years) and a relative biological activity factor of 5.

The FEEDAP Panel notes that the NDA Panel of EFSA has revised the UL levels for Vitamin D_3 for all age groups (EFSA NDA Panel, 2012, 2018): 25 μg/day for children up to 6 months, 35 μg/day for children 6–12 months, 50 μg/day for children 1–10 years and 100 μg/day for adolescents (11–17 years) and adults, including pregnant women.

In its previous opinion of 2009, the FEEDAP Panel conducted a 'worst-case scenario' exposure assessment for the consumer, based on the consumption model described in Regulation (EC) No 429/2008 and on data from studies done with the additive at the maximum use levels for pigs and poultry species. The results indicated that exposure of adults was below the provisional UL for 25-OH-D_3 set for adults (69%) but that that of children would be exceeded (138%). A refined calculation of exposure based on more realistic data (SCOOP) indicated that exposure for both adults and children would be below the provisional UL (24% and 49%, respectively). Based on that, the Panel concluded that the total exposure resulting from the use of 25-OH-D_3 in all poultry and pig categories at the maximum doses would not represent a risk for the consumer.

The FEEDAP Panel would like to withdraw the provisional UL for 25-OH-D_3, since also cholecalciferol from other food and body's own synthesis would enter the body's store of 25-OH-D_3. It is therefore considered reasonable to apply the UL for vitamin D_3 and to introduce the 25-OH-D_3 intake multiplied with a biopotency factor of 5.

In reassessing consumer exposure, the FEEDAP Panel is aware of the ongoing evaluation by the NDA Panel of setting a conversion factor for 25-OH-D_3 into vitamin D_3. At the time of the adoption of the current FEEDAP Panel's scientific opinion, the work of the NDA Panel has not been completed. Therefore, as a pragmatic approach, the Panel considers that the residues of 25-OH-D_3 deposited in edible tissues and products should be expressed in terms of vitamin D_3 activity, and therefore, multiplied by 5 to consider the relative biological activity of the different compounds. This was then compared with the UL established by the NDA Panel for vitamin D_3.

No new data have been made available in the context of the application for renewal of the authorisation with regards the deposition of 25-OH-D_3 in tissues or products of pigs or poultry not already considered in the past. The Panel is aware of ongoing applications[26] for the authorisation for use of 25-OH-D_3 for other animal species, namely ruminants, and considers that the consumer exposure assessment should cover the currently authorised uses and those covered by the ongoing applications. In that regard, the FEEDAP Panel recently adopted an opinion on the use of 25-OH-D_3 produced by a different production strain (*Pseudonocardia autotrophica* DSM 32858) in pigs and poultry. In that opinion, the FEEDAP Panel conducted a comprehensive consumer exposure calculation based on more recent data on the deposition of 25-OH-D_3 in food products from chickens for fattening and on food products from ruminants (EFSA FEEDAP Panel, 2023). The FEEDAP Panel considers that the exposure assessment performed in that opinion applies to the current assessment of the renewal of the authorisation for pigs and poultry, as it also considers the exposure from possible new uses (ruminants).

[25] Supplementary information September 2021/Appendix 1–4.
[26] FAD-2021-0064 and FAD-2021-0057.

Based on the updated consumer exposure calculation and considering the updated UL for vitamin D_3, the Panel concludes that the contribution to consumer exposure to Vitamin D_3 from products of animals fed with 25-OH-D_3 is well below the UL (11.2% to 38.58%). Therefore, the use of 25-OH-D_3 under the currently authorised conditions of use remains safe for the consumer.

3.2.3. Conclusions on safety

Based on the above and considering that the production strain qualifies for the QPS approach to safety assessment, that the genetic modifications are of no concern as regards to the toxicological profile of the production strain and that the manufacturing process, the composition of the additive and its conditions of use have not been modified, the Panel considers that there is no evidence to reconsider the conclusions reached in the previous assessments. Therefore, the FEEDAP Panel concluded that 25-hydroxycholecalciferol remains safe for the target species, the consumer and the environment under the existing conditions of the authorisation. The additive is not irritant to the skin or eyes but no conclusion on its potential to be a skin sensitiser or on its effects on the respiratory system can be reached due to absence of data.

3.3. Efficacy

The present application for renewal of the authorisation does not include a proposal for amending or supplementing the conditions of the original authorisation that would have an impact on the efficacy of the additive. Therefore, there is no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

3.4. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[27] and Good Manufacturing Practice.

4. Conclusions

The applicant provided data demonstrating that the additive currently in the market complies with the conditions of authorisation.

The FEEDAP Panel concludes that the additive does not give raise to any safety concern regarding the production strain.

Considering that the manufacturing process, the composition of the additive and its conditions of use have not been modified, the Panel considers that there is no evidence to reconsider the conclusions reached in the previous assessments. Therefore, the FEEDAP Panel concludes that 25-OH-D_3 remains safe for the target species, the consumer and the environment under the existing conditions of the authorisation. The additive is not irritant to the skin or eyes but no conclusion on its potential to be a skin sensitiser or on its effects on the respiratory system can be reached due to absence of data.

There is no need to assess the efficacy of the additive in the context of the renewal of the authorisation.

5. Recommendations

The Panel considers that in the description of the additive the term 'other related sterols' should be substituted by 'other sterol derivatives'.

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Abbreviations

BHT	butylated hydroxytoluene
CAS	Chemical Abstracts Service
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Chemical Substances
EMA	European Medicines Agency
EURL	European Union Reference Laboratory

FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
IUPAC	International Union of Pure and Applied Chemistry
LOD	limit of detection
LOQ	limit of quantification
NDA	EFSA Scientific Panel on Nutrition, Novel Food and Food Allergens
PCDD	Polychlorinated dibenzo-*p*-dioxin
PCDF	polychlorinated dibenzofuran
QPS	qualified presumption of safety
SEM	scanning electron microscopy
TEQ	toxic equivalents
WHO	World Health Organization