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Safety and efficacy of Avizyme[®] 1505 (endo-1,4-beta-xylanase, subtilisin and alpha-amylase) for all poultry species

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Abstract

Avizyme[®] 1505 is based on three enzyme activities produced by three genetically modified microorganisms: xylanase, subtilisin and amylase produced by *Trichoderma reesei*, *Bacillus subtilis* and *Bacillus amyloliquefaciens*, respectively. It is authorised for use in chickens and turkeys for fattening, ducks and laying hens. This scientific opinion concerns the request for the renewal of the authorisation of the additive for the species/categories for which there is an authorisation, a reduction of the minimum recommended level in turkeys for fattening and the extension of use to all avian species for laying, for fattening, reared for breeding and reared for laying (except for ducks). Based on recent data, uncertainty remains in the characterisation of the production strains and the possible presence in the final product of viable production strains and their DNA. Therefore, the EFSA Panel on Additives and products or Substances used in Animal Feed (FEEDAP) could not confirm the conclusions previously drawn regarding the safety of Avizyme[®] 1505 for the target species, consumers, users and environment. This conclusion applies also to the new target species for which a request for an extension of use is made. There was no need for assessing the efficacy of the additive in the context of the renewal of the authorisation for chickens for fattening, ducks and laying hens. The efficacy data previously evaluated allowed the Panel to conclude that the additive has the potential to be efficacious at 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg complete feed for all avian species for fattening (including turkeys), reared for breeding and reared for laying and 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg complete feed in all avian species for laying.

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7. Also, Article 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States. In addition, Article 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest one year before the expiry date of the authorisation.

The European Commission received a request from Danisco (UK) Ltd.² for the authorisation of a new use, a modification of the current authorisation and renewal of the authorisation of the product Avizyme[®] 1505 (endo-1,4-beta-xylanase, subtilisin and alpha-amylase), when used as a feed additive for all poultry species, (category: zootechnical additives; functional group: digestibility enhancers).

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 4(1) (authorisation of a feed additive or new use of a feed additive), under Article 13(3) (modification of the authorisation of a feed additive) and under Article 14(1) (renewal of the authorisation). The particulars and documents in support of the application were considered valid by EFSA as of 11 February 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 Avizyme[®] 1505 (endo-1,4-beta-xylanase, subtilisin and alpha-amylase), when used under the proposed conditions of use (see Section 3.1.1).

1.2. Additional information

The additive Avizyme[®] 1505 is a preparation of endo-1,4-beta-xylanase produced by a genetically modified strain of *Trichoderma reesei* (ATCC PTA 5588), subtilisin produced by a genetically modified strain of *Bacillus subtilis* (ATCC 2107) and alpha-amylase produced by a genetically modified strain of *Bacillus amyloliquefaciens* (ATCC 3978).

The additive is authorised to be used in feed for chickens for fattening, ducks, turkeys for fattening³ and laying hens.⁴

EFSA has issued three opinions on the safety and efficacy of this additive, one for chickens for fattening and ducks for fattening (EFSA, 2009b), one for turkeys for fattening (EFSA, 2009a) and one for laying hens (EFSA FEEDAP Panel, 2011).

The applicant has requested for the renewal of the authorisation for Avizyme[®] 1505 for the species/categories for which there is an authorisation. Moreover, the applicant has requested for a reduction of the minimum recommended level in turkeys for fattening (from 300 U endo-1,4-beta-xylanase, 4,000 U subtilisin and 400 U alpha-amylase/kg feed to 187.5 U endo-1,4-beta-xylanase, 2,500 U subtilisin and 250 U alpha-amylase/kg feed) and for an extension of use of the additive to all avian species for laying, for fattening, reared for breeding and reared for laying (except for ducks).

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 Danisco (UK) Ltd. (trading as Danisco Animal Nutrition) Represented by Genecor International B.V., PO Box 777, SN8 1XN, Marlborough, Wiltshire, United Kingdom.

³ Commission Regulation (EC) No 1087/2009 of 12 November 2009 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (ATCC PTA 5588), subtilisin produced by *Bacillus subtilis* (ATCC 2107) and alpha-amylase produced by *Bacillus amyloliquefaciens* (ATCC 3978) as a feed additive for chickens for fattening, for ducks and for turkeys for fattening (holder of authorisation Danisco Animal Nutrition, legal entity Finnfeeds International Limited). OJ L 297, 13.11.2009. p. 4.

⁴ Commission Implementing Regulation (EU) No 389/2011 of 19 April 2011 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase, subtilisin and alpha-amylase as a feed additive for laying hens (holder of authorisation Danisco Animal Nutrition). OJ L 104, 19.4.2011. p. 7.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁵ in support of the authorisation request for the use of Avizyme[®] 1505 as a feed additive.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, as in previous risk assessments by EFSA, to deliver the present output.

During the assessment it was noted that the definition of the xylanase unit activity in the technical dossier was different to the one in the previously evaluated method (Application FAD-2009-0006).⁶ The applicant expressed the will to modify the definition of those units according to the method used for the control of the additive evaluated in the context of another application (FAD-2010-0007).⁷ However, the validity of the methods proposed by the applicant has not been evaluated in the context of this application.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Avizyme[®] 1505 is in line with the principles laid down in Regulation (EC) No 429/2008⁸ and the relevant guidance documents: Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008), Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c) and Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b).

3. Assessment

This assessment regards the renewal of the authorisation of Avizyme[®] 1505 (endo-1,4-beta-xylanase (EC 3.2.1.8), subtilisin (EC 3.4.21.62) and alpha-amylase (EC 3.2.1.1)) when used as a zootechnical additive (functional group of digestibility enhancers) for chickens for fattening, ducks, turkeys for fattening and laying hens. It also regards the request to modify of the terms of the authorisation for turkeys for fattening and the request for an extension of use to all avian species for laying, for fattening, reared for breeding and reared for laying (except for ducks).

3.1. Characterisation

The additive Avizyme[®] 1505 (endo-1,4-beta-xylanase, xylanase; subtilisin; and alpha-amylase, amylase) is authorised in a powder form.

The information submitted regarding the manufacturing of the additive [REDACTED]

[REDACTED] The Panel considers that these modifications will not significantly modify the final product. The applicant declares that no antibiotics are used during the manufacturing process.¹⁰

The product contains the active substances [REDACTED]

⁵ FEED dossier reference: FAD-2018-0084.

⁶ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2009-0006.pdf>

⁷ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0007.pdf>

⁸ 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.

¹⁰ [REDACTED] Technical dossier/Section II/Annex II 12.

The composition of the additive has not changed since its original authorisation.

Avizyme[®] 1505 is authorised at a minimum guaranteed enzyme activity of 1,500 U xylanase/g, 20,000 U subtilisin¹² /g and 2,000 U amylase¹³ /g. The batch to batch variation was studied in three recent batches. The mean enzyme activities were 5,654 U/g for xylanase (range 5,089–5,988 U/g), 25,314 U/g for subtilisin (range 22,758–26,699 U/g) and 8,172 U/g for amylase (range 7,551–8,482 U/g).¹⁴

In the authorisation Regulations, the Units of activity for the xylanase are defined as follow: '1 U of endo-1,4-β-xylanase is the amount of enzyme that liberates 0,5 μmol of reducing sugar (xylose equivalents) per minute from a cross-linked oat spelt xylan at pH 5,3 and 50°C'. In the context of the present application, the applicant has proposed a new definition of the xylanase activity: 'one xylanase unit is the amount of enzyme that releases 0.48 μmol of reducing sugar equivalents (expressed as xylose by the DNS reducing sugar method) from wheat arabinoxylan per min at pH 4.2 and 50°C'. However, the Panel notes that its correspondence with the previous definition has not been established.

Three batches of Avizyme[®] 1505 were analysed for chemical and microbiological contamination.¹⁵ The analysis of chemical contamination included arsenic (< LOQ), cadmium (0.02–0.04 mg/kg), lead (< LOQ), mercury (< LOQ), copper (4.1–4.4 mg/kg), fluoride (< LOQ), nickel (0.2 mg/kg), phosphorus (3,200–3,600 mg/kg), selenium (< LOQ), zinc (23–26 mg/kg) and dioxins (polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/F)) 0.065 ng WHO-PCDD/F-TEQ/kg. The following toxins and mycotoxins were determined: HT-2 (< LOQ), T-2 toxin (< LOQ except for 18 μg/kg in one batch), aflatoxin B1 (< LOQ), aflatoxin B2 (< LOQ), aflatoxin G1 (< LOQ), aflatoxin G2 (< LOQ), deoxynivalenol (97–250 μg/kg), ochratoxin A (< LOQ) and zearalenone (< 10 μg/kg).¹⁶ Moreover, three batches of Avizyme[®] 1505 were analysed for the presence of

The same three batches used for the chemical contamination were analysed for microbial contamination and the analysis included *Salmonella* spp. (not detected in 25 g), *Escherichia coli* (< 10 colony forming units (CFU)/g), total aerobic count (< 150,000 CFU/g) and total coliforms (< 100 CFU/g). Three batches of the additive¹⁸ were analysed for *Salmonella* spp. (not detected in 25 g), Enterobacteriaceae (< 200 CFU/g in two batches and > 15,000 CFU/g in one batch), presumptive *Bacillus cereus* (≤ 50 CFU/g), moulds (≤ 500 CFU/g), yeasts (≤ 1,000 CFU/g) and *E. coli* (not detected in 25 g).

No antimicrobial activity was detected in three batches of Avizyme[®] 1505 analysed

Avizyme[®] 1505 is a light brown fine granular powder with a bulk density of 847 kg/m³ and shows no dusting potential (Stauber–Heubach method).^{21,22} Three batches of the additive were analysed for particle size distribution by laser diffraction and less than 12% of the particles in the product have a diameter below 100 μm, 5% particles below 50 μm and 1% below 10 μm.²³

The three enzymes present in the additive are produced by three genetically modified micro-organisms deposited at the Westerdijk Fungal Biodiversity Institute: xylanase is produced by

¹² One subtilisin (protease) unit is defined as the amount of enzyme, which liberates 2.3 micrograms of phenolic compound (expressed as tyrosine equivalents), per minute from a casein substrate at pH 10.0 and 50°C.

¹³ One alpha-amylase unit is defined as the amount of enzyme, which liberates 1 micromole of glucosidic linkages, per minute from a water insoluble cross-linked starch polymer substrate at pH 6.5 and 37°C.

¹⁴ Technical dossier/Section II/Annex II 4.

¹⁵ Technical dossier/Section II/Annex II 5.

¹⁶ LOQ: 0.1 mg/kg for arsenic; 0.01 mg/kg for cadmium; 0.05 mg/kg for lead; 0.005 mg/kg for mercury; 0.1 mg/kg for copper; 1 mg/kg for fluoride; 0.1 mg/kg for nickel; 3 mg/kg for phosphorus; 0.2 mg/kg for selenium; 0.5 mg/kg for zinc; 0.5 μg/kg for aflatoxin B1, B2, G1, G2; 20 μg/kg for deoxynivalenol (LOD 7 μg/kg); 10 μg/kg for HT-2 toxin (LOD 3 μg/kg); 1 μg/kg for ochratoxin A; 10 μg/kg for T-2 toxin (LOD 3 μg/kg); 20 μg/kg for zearalenone (LOD 7 μg/kg); 10 μg/kg acrylamide.

¹⁸ Technical dossier/Section II/Annex II 5.

²¹ Technical dossier/Section II/Annex II 14.

²² Technical dossier/Section II/Annex II 16.

²³ Technical dossier/Section II/Annex II 15.

Trichoderma reesei CBS 143953 (formerly deposited at the American Type Culture Collection (ATCC) PTA 5588), subtilisin is produced by *Bacillus subtilis* CBS 143946 (formerly ATCC 2107) and amylase is produced by *B. amyloliquefaciens* CBS 143954 (formerly ATCC 3978). ■

Trichoderma reesei CBS 143953 – production strain of the xylanase

The taxonomic identification of the recipient strain [REDACTED]

as *T. reesei* was confirmed [REDACTED]

[REDACTED] However, the analysis was not conducted on the production strain. Therefore, the Panel has some reservations regarding the data used for the species assignment of the production strain *T. reesei* CBS 143953. *T. reesei* CBS 143953 was developed from [REDACTED]

[REDACTED] The assessment of the genetic modification of the production strain was performed in a previous evaluation (EFSA, 2009b) and the Panel concluded that the genetic modification of the xylanase production strain does not raise any safety concern. The production strain has not been subject to any further genetic modification. [REDACTED]

[REDACTED] However, no data on the ability of the production strain to produce mycotoxins was provided.

Bacillus subtilis CBS 143946 – production strain of the subtilisin

The intermediate strain [REDACTED]

[REDACTED] However, the analysis was not conducted on the production strain (CBS 143946). Therefore, the Panel has some reservations regarding the data used for the species assignment of the production strain *B. subtilis* CBS 143946. The subtilisin production strain is a derivative of [REDACTED]

[REDACTED] The assessment of the genetic modification of the production strain was performed in a previous assessment (EFSA, 2009b) and the Panel concluded that the production strain [REDACTED] [REDACTED] The production strains have not been subject to any further genetic modification.

The susceptibility of *B. subtilis* CBS 143946 to the antibiotics recommended by FEEDAP was tested [REDACTED]

[REDACTED] FEEDAP cut-off values (EFSA FEEDAP Panel, 2018a). [REDACTED]

The whole genome sequence (WGS) of the strain [REDACTED]

[REDACTED] However, the genome of the production strain was not searched for genes conferring resistance to antimicrobials. Therefore, uncertainty remains on the possible presence of acquired antimicrobial resistance genes [REDACTED] in the *B. subtilis* CBS 143946 production strain.

The toxigenic potential of the strain [REDACTED]

[REDACTED] However, no new data on the toxigenic potential of the production strain *B. subtilis* CBS 143946 was provided [REDACTED]

Bacillus amyloliquefaciens CBS 143954 – production strain of the amylase

The production strain *B. amyloliquefaciens* CBS 143954 has been confirmed as *B. amyloliquefaciens*

[REDACTED] The amylase production organism is a derivative of [REDACTED]

[REDACTED] The assessment of the genetic modification of the production strain was performed in a previous assessment (EFSA, 2009b) and the Panel concluded the production strain [REDACTED] The production strain has not been subject to any further genetic modification.

The susceptibility of *B. amyloliquefaciens* CBS 143954 to the antibiotics recommended by FEEDAP was tested [REDACTED]

[REDACTED] the FEEDAP cut-off values (EFSA FEEDAP Panel, 2018a).

The applicant briefly described the search of the WGS of the production strain *B. amyloliquefaciens* CBS 143954 [REDACTED]

[REDACTED] The Panel notes that the analysis was poorly reported and that the results should have been further described.

The toxigenic potential of *B. amyloliquefaciens* CBS 143954 was assessed [REDACTED]

[REDACTED] so *B. amyloliquefaciens* CBS 143954 is considered to be not toxigenic.

B. amyloliquefaciens CBS 143954 was also tested [REDACTED]

Presence of viable cells and DNA of the production strains in the final product

The applicant provided two sets of data regarding the presence of viable cells of the production strains in the additive. In the first set of data

[REDACTED]

In a second analysis, the presence of the production strains was tested

[REDACTED]

Consequently, considering the low sensitivity of the two analyses performed, uncertainty remains on the presence of viable cells of the production strains in the additive.

The presence of recombinant DNA from the three production strains was analysed in triplicate in three batches

[REDACTED]

Uncertainty remains on the sensitivity of the methods and does not allow the FEEDAP Panel to exclude the presence of DNA from the production strains in the product.

[REDACTED]

uncertainty remains on the presence of DNA fragments that could encode for antimicrobial resistance genes in the final product which would be of concern.

3.1.1. Conditions of use

The additive is currently authorised for use in feed as a feed additive for the target species as follows:

- 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg of complete feed for chickens for fattening,
- 75 U xylanase, 1,000 U subtilisin and 100 U amylase/kg of complete feed for ducks,
- 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed for turkeys for fattening and laying hens.

[REDACTED]

The applicant has not asked to modify these conditions of use except for turkeys for fattening, for which has asked to reduce the minimum recommended level to 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg feed.

In addition, the applicant proposed the extension of use as follows:

- 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg of complete feed for all avian species for fattening, reared for breeding and reared for laying (except for ducks)
- 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed for all avian species for laying (except for ducks).

In the other provisions of the authorisation is specified that 'For safety reasons: breathing protection, glasses and gloves shall be used during handling. An appropriate method for control purposes shall be developed'.

3.2. Safety

In the previous assessments (EFSA, 2009a,b; EFSA FEEDAP Panel, 2011) and based on the data and knowledge available at that time, the FEEDAP Panel concluded that no DNA and no cells were present in the additive, that the use of the product as a feed additive is safe for the target species, the consumers of products derived from animals fed with the additive, and for the environment. The Panel also concluded that the additive is a mild irritant to skin and eyes; it is not a dermal sensitiser but should be considered a potential respiratory sensitiser.

In line with the requirements established in the EFSA guidance on the renewal (EFSA FEEDAP Panel, 2013), the applicant performed a literature search in order to provide evidence that in the light of the current knowledge the additive remains safe under the approved conditions for target species, consumers, users and the environment. The applicant searched in a total of 3 relevant databases (CAB Abstracts, Veterinary Science Database and Medline).^{42,43,44} The search covered the period 2009–2018 (from 2009 to November 2017 for xylanase), was restricted to publications in English language and the search terms and search strategy were provided. The main search terms were 'xylanase', 'amylase' and 'subtilisin' and included terms relevant for target species safety and for toxicological aspects.

The literature search retrieved 347, 14 and 49 publications for xylanase, amylase and subtilisin respectively. Most of the publications (339, 11 and 46 for xylanase, amylase and subtilisin respectively) were excluded from the assessment because the product was not the one under assessment or the safety of the product was not assessed. The other publications found did not report any safety issues, therefore were considered not relevant.

The applicant stated that no adverse events have been detected under its global monitoring plan.⁴⁵

The data newly provided to confirm the identification of the xylanase production strain *T. reesei* CBS 143953 allow to unambiguously identify the parental strain as *T. reesei*. The lack of mycotoxigenic potential has not been demonstrated for this production strain.

The identity of the intermediate strain of the production strain *B. subtilis* CBS 143946 has been conclusively established. However, no new data on the toxigenic potential of the production strain *B. subtilis* CBS 143946 was provided. *B. subtilis* CBS 143946 shows [REDACTED]

With regard to *B. amyloliquefaciens* CBS 143954, its identity has been unambiguously established and evidence that the strain lacks toxigenic potential has been demonstrated. *B. amyloliquefaciens* CBS 143954 shows [REDACTED]

The production strains are genetically modified, [REDACTED]

[REDACTED] Uncertainty remains on the possible presence of viable cells from the production strains and their recombinant DNA in the product. Therefore, the Panel considers that the information provided by the applicant does not fulfil the minimum requirements to support that the additive remains safe under the approved conditions for target species, consumers, users and the environment.

⁴² Technical dossier/Section III/RCVS 2017.

⁴³ Technical dossier/Section III/RCVS 2018a.

⁴⁴ Technical dossier/Section III/RCVS 2018b.

⁴⁵ Technical dossier/Section III/Annex III.1.

3.3. Efficacy

The efficacy of Avizyme[®] 1505 was previously established in chickens for fattening at 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg of complete feed and in ducks at 75 U xylanase, 1,000 U subtilisin and 100 U amylase/kg of complete feed (EFSA, 2009b). In laying hens, it was established at 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed (EFSA FEEDAP Panel, 2011). The conditions of use for these target species have not been modified and therefore no further assessment is needed for the renewal of the authorisation in these species.

The applicant has now requested to reduce the recommended level in feed for turkeys for fattening to 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg feed, which was previously established at 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed (EFSA, 2009a).

In addition, the applicant proposed the extension of use to all avian species for fattening, reared for breeding and reared for laying (except for ducks) at the level of 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg of complete feed and to all avian species for laying (except for ducks) at a minimum recommended level of 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed.

Considering that efficacy has been demonstrated in chickens for fattening and in laying hens at the doses of 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase/kg of complete feed and 300 U xylanase, 4,000 U subtilisin and 400 U amylase/kg of complete feed, respectively, and the fact that the mode of action of the enzymes present in the additive can be reasonably assumed to be the same in the different poultry species, the conclusions from the efficacy studies in chicken for fattening can be extended/extrapolated to all avian species for fattening, reared for breeding and reared for laying (except for ducks). In a similar way, the conclusions from the efficacy in laying hens can be extended/extrapolated to all avian species for laying (except for ducks). Therefore, the Panel considers that the additive has the potential to be efficacious in these species at the proposed conditions of use.

However, the Panel notes that due to the modification in the definition of the xylanase activities and the lack of data regarding the relationship with the activity previously defined, uncertainty remains on the minimum actual xylanase activity that would correspond to the enzyme activity currently authorised.

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 Regulation⁴⁶ and Good Manufacturing Practice.

3.5. Conclusions

The applicant has not provided enough evidence that the additive complies with the conditions of the authorisation.

Considering the uncertainties in the characterisation of the production strains and the possible presence in the final product of viable production strains and their DNA, the FEEDAP Panel cannot confirm the previously drawn conclusions regarding the safety of Avizyme[®] 1505 for the target species, consumers, users and environment. This conclusion applies also to the new target species for which a request for an extension of use is made (all avian species for fattening, reared for breeding and reared for laying and all avian species for laying).

There is no need for assessing the efficacy of Avizyme[®] 1505 in the context of the renewal of the authorisation in chickens for fattening, ducks and laying hens. The Panel concludes that the additive has the potential to be efficacious in turkeys for fattening, all avian species for fattening, reared for breeding and reared for laying at 187.5 U xylanase, 2,500 U subtilisin and 250 U amylase per kg of complete feed and at 300 U xylanase, 4,000 U subtilisin and 400 U amylase per kg of complete feed for all avian species for laying (except for ducks).

⁴⁶ Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 October 2003 laying down requirements for feed hygiene. OJ L 282, 24.10.2003, p. 1.

3.6. Recommendation

The Panel notes that the applicant has proposed a new definition for the units of xylanase which is different than the one currently described in the authorisation. Although the applicant states that such method has already been evaluated in the context of another application, the applicability of such method in the context of the present application has not been assessed. The Panel recommends that the method proposed by the applicant to analyse the xylanase activity should be evaluated in the context of the application for renewal of the authorisation.

Chronology

Date	Event
28/11/2018	Dossier received by EFSA
19/12/2018	Reception mandate from the European Commission
11/02/2019	Application validated by EFSA – Start of the scientific assessment
18/03/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: characterisation, safety</i>
11/05/2019	Comments received from Member States
19/09/2019	Reception of supplementary information from the applicant - Scientific assessment re-started
30/01/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ATCC	American Type Culture Collection
CFU	colony forming unit

EC	Enzyme Commission
FEEDAP EFSA	Panel on Additives and Products or Substances used in Animal Feed
LOQ	limit of quantification
PCDD/F	polychlorinated dibenzo- <i>p</i> -dioxins and dibenzofurans
TEQ	toxic equivalent
WGS	whole genome sequence
WHO	World Health Organization