SCIENTIFIC OPINION

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Safety and efficacy of ZM16 10 (*Bacillus amyloliquefaciens* DSM 25840) as a feed additive for sows in order to have benefits in piglets, sows for reproduction, piglets (suckling and weaned), pigs for fattening and minor porcine species

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Abstract

Following a request from the European Commission, the EFSA Panel on Additives and products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of ZM16 10 for all pigs. The additive is a preparation containing viable spores of a strain of *Bacillus amyloliquefaciens* intended for use in feed at the proposed dose of 5×10^8 CFU/kg complete feedingstuffs and in water for drinking at 1.7×10^8 CFU/L. The additive exists in two forms, ZM16 and ZM16 10, and has been previously characterised by the FEEDAP Panel. *B. amyloliquefaciens* is considered by EFSA to be suitable for the qualified presumption of safety (QPS) approach to establishing safety. The active agent fulfils the requirements and consequently, the additive was presumed safe for the target animals, consumers of products from treated animals and the environment. Given the proteinaceous nature of the active agent, the additive should be considered a potential respiratory sensitiser. In the absence of data, the FEEDAP Panel cannot conclude on the irritancy potential of the additive to skin and eyes or its dermal sensitisation. The data made available by the applicant allowed the Panel to conclude that the additive, in either form, has a potential to be efficacious as a zootechnical additive when added to feed for piglets (suckling and weaned), pigs for fattening and sows at 5×10^8 CFU/kg (corresponding to 1.7×10^8 CFU/L). The conclusions on the efficacy were extrapolated to all Suidae species.

Keywords: zootechnical additive, digestibility enhancers, *Bacillus amyloliquefaciens*, safety, QPS, efficacy, pigs

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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 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.

The European Commission received a request from Chr. Hansen A/S[2] for authorisation of the product ZM16 10[3] (*Bacillus amyloliquefaciens* DSM 25840), when used as a feed additive for sows, piglets, pigs for fattening and minor porcine species (category: Zootechnical additives; functional group: gut flora stabilisers).

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). The particulars and documents in support of the application were considered valid by EFSA as of 16 October 2018.

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 ZM16 10 (*B. amyloliquefaciens* DSM 25840), when used under the proposed conditions of use (see Section 3.1).

1.2. Additional information

The additive ZM16 10 is a preparation containing viable spores of *B. amyloliquefaciens* DSM 25840 that has not been previously authorised as a feed additive in the European Union. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) adopted an opinion on the safety and efficacy of ZM16 10 when used with weaned piglets and weaned minor porcine species (EFSA FEEDAP Panel, 2018a). In that instance, the issues relating to characterisation and safety of the additive for the target species, consumers of products derived from treated animals and the environment were satisfactorily addressed, but no conclusions could be drawn on the efficacy of the additive for the target species.

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[4] in support of the authorisation request for the use of ZM16 10 (*B. amyloliquefaciens* DSM 25840) as a feed additive.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[5]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the efficacy of ZM16 10 is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Technical guidance: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011) and Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b).

[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] Chr. Hansen A/S, 10-12 Boege Allé, 2970 Hoersholm, Denmark.
[3] The applicant declared to intend to market the product with other tradenames.
[4] FEED dossier reference: FAD-2018-0056.
[5] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/finrep-fad-2016-0069_bacillus_amylo.pdf
[6] 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.

3. Assessment

ZM16 10 is a preparation of viable spores of *B. amyloliquefaciens* intended to be used as a zootechnical additive (functional group: digestibility enhancers) for all pigs and minor porcine species.

3.1. Characterisation

The additive ZM16 10 is a preparation of a non-genetically modified strain deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen with the accession number DSM 25840. In a previous assessment the FEEDAP Panel (EFSA FEEDAP Panel, 2018a,b) characterised the strain and the additive and no new information has been provided. The strain was taxonomically identified as *B. amyloliquefaciens* by molecular techniques; it was shown to be susceptible to the relevant antibiotics and not toxigenic.

The additive under assessment has the same composition (spores concentrate (3%), carrier (calcium carbonate, 96 %) and an anticaking agent (kieselgur,[7] 1 %), and method of manufacture as those considered in the previous application. It ensures a minimum guaranteed concentration of 1.25×10^{10} coliforms forming units (CFU)/g additive. The applicant mentions in the dossier a second formulation called ZM16 and with a minimum concentration of 1.25×10^{9} CFU/g additive, [redacted] This form was used in all the efficacy studies (Section 3.3). The two forms are considered equivalent when delivering the same dose. The data pertaining to composition, physical properties and stability submitted in the previous application dossier still apply.

The additive is intended to be used in feed and water for drinking for piglets (suckling and weaned), pigs for fattening, sows (for reproduction or to have a benefit in piglets) and other minor porcine species at 5×10^{8} CFU/kg complete feedingstuffs or 1.7×10^{8} CFU/L of drinking water.

3.2. Safety

The bacterial species *B. amyloliquefaciens* is considered by EFSA to be suitable for the qualified presumption of safety (QPS) approach to safety assessment (EFSA, 2007; EFSA BIOHAZ Panel, 2017). This approach requires the identity of the strains to be conclusively established and evidence that the strains lack toxigenic potential and do not show resistance to antibiotics of human and veterinary importance. In the context of a previous opinion (EFSA FEEDAP Panel, 2018a,b), the identification of the strain and compliance with the QPS qualifications were confirmed. Therefore, the Panel concluded that *B. amyloliquefaciens* DSM 25840 can be presumed safe for target animals, consumers of products derived from animals fed the additive and the environment. The substances used in the formulation of the additive would not modify these conclusions. In the previous opinion, the Panel concluded that the additive should be considered a potential respiratory sensitiser. In the absence of data, the FEEDAP Panel could not conclude on the irritancy potential of the additive to skin and eyes or its dermal sensitisation.

No new information has been made available that would lead the FEEDAP Panel to reconsider the conclusion previously drawn. Moreover, the use of the additive in the new target species/categories would not introduce hazards/risks not already considered.

In the previous opinion (EFSA FEEDAP Panel, 2018a,b), ZM16 10 was considered a potential respiratory sensitiser, but no conclusions could be drawn on its irritancy potential to skin and eyes or its dermal sensitisation, due to lack of data. No new information supporting safety of the additive for the user has been submitted in the current application.

3.3. Efficacy

3.3.1. Efficacy for weaned piglets

The data submitted in the present application were already evaluated in a previous assessment (EFSA FEEDAP Panel, 2019). Based on the results of a statistical analysis pooling the data of four trials, the Panel concluded that the additive has the potential to be efficacious as a zootechnical additive in weaned piglets at 5×10^{8} CFU/kg complete feed (corresponding to 1.7×10^{8} CFU/L of drinking water).

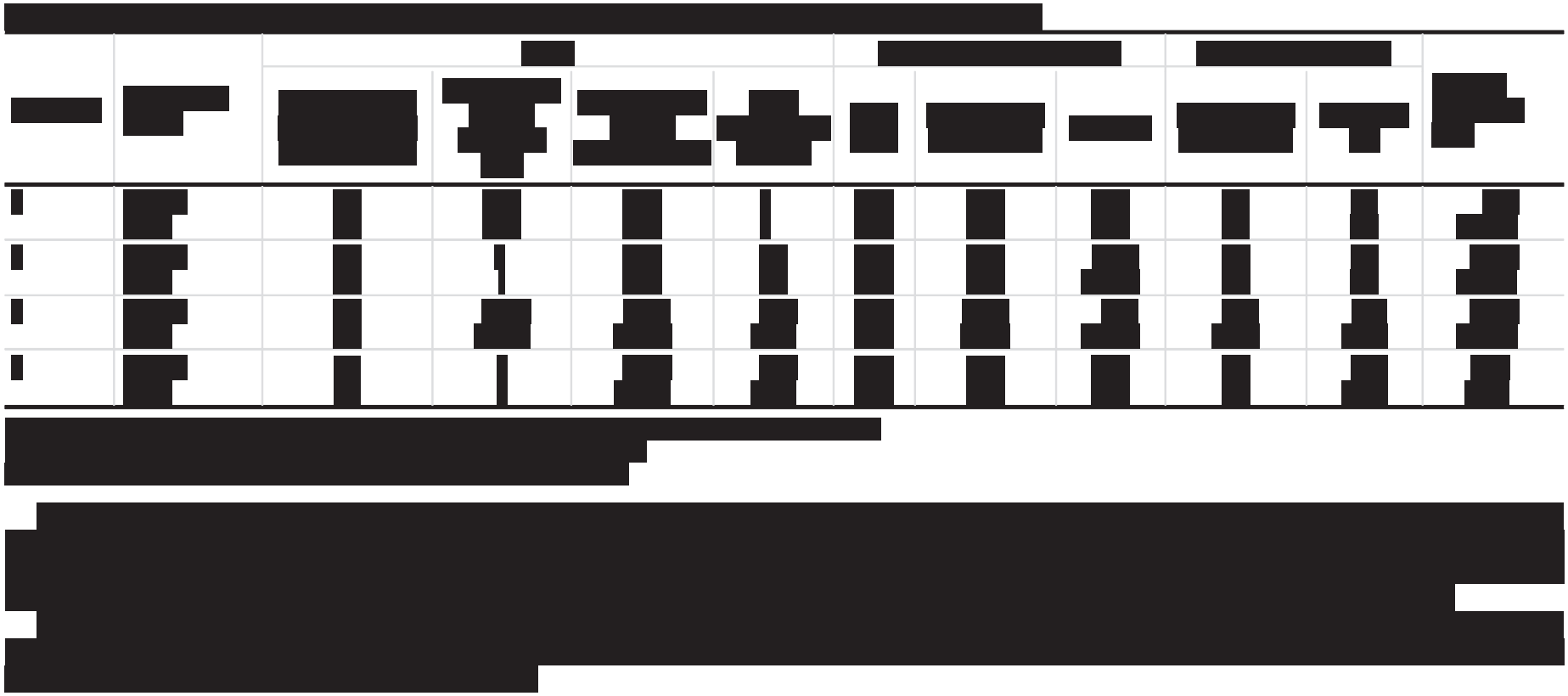
[7] Currently under re-evaluation according to Article 10(2) of Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

3.3.2. Efficacy for pigs for fattening

A total of four trials with pigs for fattening were submitted. All four studies shared a common design and the data of the four studies were pooled in a joint statistical analysis. Two of the trials were not considered as independent because were they done in the same trial site, using the same feed and overlapping in time. However, the data of the two trials were considered in the assessment as one unique trial (Trial 1 in tables). The statistical analysis of the data from the four studies initially submitted was not considered further in the assessment because only three independent studies were available.

3.3.3. Efficacy for sows

A total of six studies in sows that shared a similar design were submitted. Three of the trials were conducted in the same place, shared diets and overlapped in time, consequently these studies were not considered independent and all these data were pooled and analysed considering them as a single study.



3.3.4. Conclusions on efficacy

The application was made for Suidae in all productive stages and studies in weaned piglets, pigs for fattening and sows (for two cycles) were submitted. The two forms of the additive are considered to be equivalent when added at the same level to water/feed.

The studies provided in weaned piglets had been assessed by the FEEDAP Panel and it was concluded that the additive has a potential to be efficacious as a zootechnical additive in weaned piglets at the recommended level of 5×10^8 CFU/kg complete feed (corresponding to 1.7×10^8 CFU/L water for drinking). This conclusion can be extended to the use of the additive in feed for suckling piglets.

The studies submitted in sows showed that the additive has a potential to be efficacious in sows and their litters at 5×10^8 CFU/kg complete feed (corresponding to 1.7×10^8 CFU/L water for drinking).

The results of the studies submitted in the current dossier are not sufficient to conclude on the efficacy of the additive in pigs for fattening. However, the Panel considers that since efficacy has been established in weaned piglets and sows, the efficacy in pigs for fattening can be assumed without the need for further data. Therefore, the Panel considers that the additive has the potential to be efficacious as a zootechnical additive in pigs for fattening at 5×10^8 CFU/kg complete feed (corresponding to 1.7×10^8 CFU/L water).

Considering that additive can be assumed to have similar effects in all Suidae species, the above conclusions are extrapolated to include all Suidae in all life stages.

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[19] and Good Manufacturing Practice.

4. Conclusions

The additive is safe for target animals, consumers of products derived from animals fed the additive and the environment.

The additive should be considered a potential respiratory sensitiser. The FEEDAP Panel cannot conclude on the irritancy potential of the additive to skin and eyes or its dermal sensitisation.

The additive, in either form, is efficacious for all Suidae in all productive stages at feed at 5×10^8 CFU/kg complete feed (corresponding to 1.7×10^8 CFU/L).

Documentation as provided to EFSA/Chronology

Date	Event
07/08/2018	Dossier received by EFSA. ZM16 10 (*Bacillus amyloliquefaciens* DSM 25840) for pigs. Submitted by Chr. Hansen A/S
04/09/2018	Reception mandate from the European Commission
16/10/2018	Application validated by EFSA – Start of the scientific assessment
19/12/2018	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: efficacy*
06/02/2019	Clarification teleconference during risk assessment with the applicant according to the "EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products"
19/02/2019	Reception of supplementary information from the applicant - Scientific assessment re-started
16/01/2019	Comments received from Member States
11/04/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: efficacy*
11/06/2019	Clarification teleconference during risk assessment with the applicant according to the "EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products"
13/08/2019	Reception of supplementary information from the applicant - Scientific assessment re-started
04/10/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

[19] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

References

EFSA (European Food Safety Authority), 2007. Opinion of the Scientific Committee on a request from EFSA on the introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. EFSA Journal 2007;5(12):587, 16 pp. https://doi.org/10.2903/j.efsa.2007.587

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Girones R, Herman L, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Ru G, Sanaa M, Simmons M, Skandamis P, Snary E, Speybroeck N, Ter Kuile B, Threlfall J, Wahlström H, Cocconcelli PS, Klein G, Prieto Maradona M, Querol A, Peixe L, Suarez JE, Sundh I, Vlak JM, Aguilera-Gómez M, Barizzone F, Brozzi R, Correia S, Heng L, Istace F, Lythgo C and Fernández Escámez PS, 2017. Scientific Opinion on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA. EFSA Journal 2017;15(3):4664, 177 pp. https://doi.org/10.2903/j.efsa.2017.4664

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011. Technical guidance: tolerance and efficacy studies in target animals. EFSA Journal 2011;9(5):2175, 15 pp. https://doi.org/10.2903/j.efsa.2011.2175

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012. Guidance for the preparation of dossiers for zootechnical additives. EFSA Journal 2012;10(1):2536, 19 pp. https://doi.org/10.2903/j.efsa.2012.2536

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, Lopez Puente S, Mantovani A, Mayo B, Ramos F, Villa RE, Wallace RJ, Wester P, Brozzi R and Saarela M, 2018a. Scientific Opinion on the safety and efficacy of ZM16 10 (*Bacillus amyloliquefaciens* DSM 25840) as a feed additive for weaned piglets and minor porcine species. EFSA Journal 2018;16(4):5200, 9 pp. https://doi.org/10.2903/j.efsa.2018.5200

EFSA FEEDAP Panel (EFSA Panel on additives and products or substances used in animal feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J, Innocenti ML and Martino L, 2018b. Guidance on the assessment of the efficacy of feed additives. EFSA Journal 2018;16(5):5274, 25 pp. https://doi.org/10.2903/j.efsa.2018.5274

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis V, Azimonti G, Bastos ML, Christensen H, Dusemund B, Kouba M, Kos Durjava M, López-Alonso M, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Anguita M, Galobart J, Holckznecht O, Manini P, Pettenati E, Pizzo F and Tarrés Call J, 2019. Scientific opinion on the efficacy of ZM16 (*Bacillus amyloliquefaciens* DSM 25840) as a feed additive for weaned piglets and minor porcine species. EFSA Journal 2019;17(10):5881, 7 pp. https://doi.org/10.2903/j.efsa.2019.5881

Abbreviations

ANOVA	analysis of variance
CFU	colony forming unit
EURL	European Union Reference Laboratory
FEEDAP	EFSA Panel on Additives and products or Substances used in Animal Feed
QPS	qualified presumption of safety