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Assessment of the application for renewal of authorisation of Bonvital® (*Enterococcus faecium* DSM 7134) as a feed additive for weaned piglets and pigs for fattening

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Abstract

Bonvital® is the trade name for a feed additive based on *Enterococcus faecium* DSM 7134 currently authorised for use in piglets, pigs for fattening, sows, chickens for fattening, chickens reared for laying and minor poultry species. This opinion concerns the renewal of the authorisation of Bonvital® as a zootechnical additive for weaned piglets and pigs for fattening. The applicant is proposing to increase the minimum and maximum inclusion level of the additive in feed for weaned piglets and the maximum for pigs for fattening. The applicant has provided data demonstrating that the additive currently in the market complies with the conditions of authorisation. *E. faecium* DSM 7134 does not belong to the hospital-associated clade and does not express resistance to the antibiotics tested; therefore, its use in animal nutrition is considered safe for the target animals and consumers of animal products. Bonvital® is also considered safe for the target animals and consumers. In previous opinions, Bonvital® was found to be non-irritant to skin and eyes, but a potential skin/respiratory sensitiser and safe for the environment. No new evidence has been identified that would make the Panel reconsider the previous conclusions on the safety of the additive. The conclusions reached before are considered to cover the higher maximum application rates proposed by the applicant. Therefore, the Panel concludes that Bonvital® used under the proposed conditions of use is safe for weaned piglets and pigs for fattening, consumers of products derived from animals fed Bonvital® and the environment. Bonvital® is considered a potential skin/respiratory sensitiser. The additional studies provided confirm that Bonvital® has the potential to be efficacious in weaned piglets at 1×10^9 colony forming unit (CFU)/kg feed and in pigs for fattening at 2×10^8 CFU/kg feed.

Keywords: Bonvital®, *Enterococcus faecium* DSM 7134, safety, efficacy, weaned piglets, pigs for fattening

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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 of that Regulation specifies that for products authorised according to Article 9, an application for renewal shall be submitted in accordance with Article 7, at the latest one year before the expiry date of the authorisation.

The European Commission received two requests from Lactosan GmbH & Co.Kg[2] for renewal of the authorisation of the product Bonvital® (*Enterococcus faecium* DSM 7134), one when used as a feed additive for weaned piglets and one for pigs for fattening (category: zootechnical additive; functional group: gut flora stabiliser).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the applications to the European Food Safety Authority (EFSA) as applications under Article 14(1) (renewal of an authorised feed additive). EFSA received directly from the applicant the technical dossiers in support of these applications. The particulars and documents in support of the applications were considered valid by EFSA as of 5 October 2016.

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 Bonvital (*Enterococcus faecium* DSM 7134), when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

EFSA issued several opinions on the product when used with chickens for fattening (EFSA, 2004), piglets and pigs for fattening (EFSA, 2007a), sows (EFSA, 2007b; EFSA FEEDAP Panel, 2014), dogs (EFSA, 2009a), chickens for fattening (EFSA, 2009b; EFSA FEEDAP Panel, 2010) and chickens reared for laying and minor avian species (EFSA FEEDAP Panel, 2013a). EFSA issued an opinion on the safety and efficacy of a microbial product containing *Enterococcus faecium* (DSM 7134) and *Lactobacillus rhamnosus* when used in feed for calves for rearing (EFSA FEEDAP Panel, 2013b).

Bonvital® is currently authorised as a zootechnical additive (functional group: gut flora stabiliser, 4b1841) for use in piglets, pigs for fattening,[3] sows,[4] chickens for fattening,[5] chickens reared for laying and minor poultry species other than those used for laying.[6] The active agent *E. faecium* DSM 7134 is also authorised in combination with *Lactobacillus rhamnosus* (DSM 7133) under a different trade name for calves for rearing.[7]

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of two technical dossiers[8] in support of the request for the use of Bonvital (*Enterococcus faecium* DSM 7134) as a feed

[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] Lactosan GmbH & Co.Kg, Industriestrasse West 5, 8605 Kapfenberg, Austria.
[3] Commission Regulation (EC) No 538/2007 of 15 May 2007 concerning the authorisation of a new use of *Enterococcus faecium* DSM 7134 (Bonvital) as a feed additive. OJ L 128, 16.5.2007, p. 16.
[4] Commission Regulation (EC) No 1521/2007 of 19 December 2007 concerning the authorisation of a new use of *Enterococcus faecium* DSM 7134 (Bonvital) as a feed additive. OJ L 335, 20.12.2007, p. 24.
[5] Commission Regulation (EU) No 998/2010 of 5 November 2010 concerning the authorisation of *Enterococcus faecium* DSM 7134 as a feed additive for chickens for fattening (holder of the authorisation Lactosan GmbH & Co KG. OJ L 290, 6.11.2010, p. 22.
[6] Commission Implementing Regulation (EU) No 775/2013 of 12 August 2013 concerning the authorisation of a preparation of *Enterococcus faecium* DSM 7134 as a feed additive for chickens reared for laying and minor poultry species other than those used for laying (holder of authorisation Lactosan GmbH & Co KG). OJ L 217, 13.8.2013, p. 32.
[7] Commission Implementing Regulation (EU) No 1101/2013 of 6 November 2013 concerning the authorisation of a preparation of *Enterococcus faecium* DSM 7134 and *Lactobacillus rhamnosus* DSM 7133 as a feed additive for calves for rearing and amending Regulation (EC) No 1288/2004 (holder of authorisation Lactosan GmbH & CoKG). OJ L 296, 7.11.2013, p. 1.
[8] FEED dossier references: FAD-2016-0038 and FAD-2016-0036.

additive. The technical dossiers were prepared following the provisions of Article 7 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008 and the applicable EFSA guidance documents.

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

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current applications.[9]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Bonvital® (*Enterococcus faecium* DSM 7134) is in line with the principles laid down in Regulation (EC) No 429/2008[10] and the relevant guidance documents: Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013c), Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012a), Guidance on the assessment of bacterial susceptibility to antimicrobials of human and veterinary importance (EFSA FEEDAP Panel 2012b), Guidance on the safety assessment of *E. faecium* in animal nutrition (EFSA FEEDAP Panel, 2012c) and Technical guidance on tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011).

3. Assessment

Bonvital® is a preparation consisting of viable cells of *E. faecium* DSM 7134, as a zootechnical additive (functional group: gut flora stabiliser) for use in piglets and pigs for fattening.

3.1. Characterisation

3.1.1. Characterisation of the additive

Bonvital® is currently authorised in two forms:

- Bonvital powder® composed of cell concentrate (3%), carrier (sweet whey powder, 96%) and other excipients (lactose 0.5%, sodium citrate 0.1%, sodium glutamate 0.1%, sodium ascorbate 0.05%, sodium lactate 0.2%, mannitol 0.05%) to reach a guaranteed minimum concentration of 1×10^{10} colony forming unit (CFU)/g, and
- Bonvital granules®, microencapsulated formula, composed of cell concentrate (3%), saccharose (70%), maltodextrin (20%), sodium citrate (1%), (sodium glutamate 1.0%, sodium ascorbate 0.5%, sodium lactate 2.5%, mannitol 1.5%, starch 0.5%) with a guaranteed minimum concentration 1×10^{10} CFU/g.

The applicant declared that the manufacturing process has not been changed and Bonvital® has not been altered in composition, purity or activity since the last authorisation, and provided data supporting it. Compliance with specifications was confirmed by analysis of three batches (from 2018) of each form (Bonvital powder®: range 1.13–1.39 $\times$ 10^{10} CFU/g, and Bonvital granules®: range 1.14–1.40 $\times$ 10^{10} CFU/g).[11]

Three batches of each form produced in 2016 were analysed for chemical and microbiological purity.[12] Results confirm compliance with action limits (Enterobacteriaceae < 1,000 CFU/g, yeasts and filamentous fungi < 1,000 CFU/g, *Salmonella* none detectable in 25 g, aflatoxins B1, B2, G1 and G2 < 0.03 μg/kg, zearalenone < 5 μg/kg, deoxynivalenol < 10 μg/kg, arsenic < 1.5 mg/kg, lead < 1.0 mg/kg, cadmium 0.1 mg/kg and mercury < 0.05 mg/kg).

[9] The full report is available on the EURL website: https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports/fad-2008-0007?search&form-return

[10] 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.

[11] Technical dossiers/Supplementary information February and March 2018/Annex Supp info_1.

[12] Technical dossier/Section II/Annexes II.1-11, II.1-12 and II.1-13.

3.1.2. Characterisation of the active agent

Enterococcus faecium DSM 7134 is deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen, under the accession number DSM 7134.[13] *E. faecium* DSM 7134 was identified by means of biochemical and genetic techniques, such as the sequence of the *rrn* operon, including the complete 16S rRNA gene, and characterised at strain level by pulsed-field gel electrophoresis (PFGE) and random amplification of polymorphic DNA (RAPD) fingerprinting techniques.[14] RAPD and PFGE profiles were used to compare the active agent with the master cell bank culture.[15] No differences in the resultant patterns were observed between the master culture and several generations of growth.

The minimum inhibitory concentration (MIC) of ampicillin for *E. faecium* DSM 7134 was 0.5 mg/L and the polymerase chain reaction (PCR) analyses demonstrated the absence of the genetic determinants IS*16*, *hyl*Efm and *esp*, typical of hospital-associated strains as required in the guidance on the safety assessment of *E. faecium* in animal nutrition (EFSA FEEDAP Panel, 2012c).[16] Therefore, *E. faecium* DSM 7134 does not contain marker genes typical of hospital-associated isolates responsible for clinical infections and is considered safe.

The strain was tested for antibiotic susceptibility using twofold broth dilutions. The battery of antibiotics tested included all of those recommended by EFSA (EFSA FEEDAP Panel, 2012b).[17] As all MIC values were equal or lower than the corresponding cut-off values defined by the FEEDAP Panel, the strain is considered susceptible to all relevant antibiotics.

3.1.3. Conditions of use

Bonvital® is currently authorised in feed for weaned piglets at the minimum dose of 5×10^8 CFU/kg complete feed and the maximum dose of 4×10^9 CFU/kg complete feed, with the recommended dose of 1×10^9 CFU/kg feed. The applicant now proposes the use at the minimum dose of 1×10^9 CFU/kg complete feed and the maximum dose of 1×10^{10} CFU/kg complete feed.

Similarly, Bonvital® is currently authorised in feed for pigs for fattening at the minimum dose of 2×10^8 CFU/kg complete feed and a maximum dose of 1×10^9 CFU/kg complete feed, with the recommended dose of 5×10^8 CFU/kg feed. The applicant now proposes to increase the maximum dose to 2×10^9 CFU/kg complete feed.

3.2. Safety

The active agent has been identified as *E. faecium.* The metabolic end products of the species are typical of lactic acid bacteria and do not raise concerns. *E. faecium* is not a recognised pathogen for pigs, lacks the marker genes associated with human clinical isolates and is susceptible to relevant antibiotics (EFSA FEEDAP Panel, 2013a). Therefore, the use of *E. faecium* DSM 7134 in animal nutrition is not expected to raise concerns for the target animals or consumers of animal products. Since neither the active agent nor the other components of the additive give rise to concerns, the FEEDAP Panel considers the use of Bonvital safe for the target animals and consumers.

In a previous opinion, Bonvital® was found to be not irritant to skin and eyes but a potential skin/respiratory sensitiser (EFSA FEEDAP Panel, 2013a,b,c). As Bonvital powder® has the potential to produce a respirable dust, it is considered more hazardous for users than the granular form.

In the same opinion, the Panel concluded that Bonvital® is safe for the environment.

In order to confirm that the additive remains safe under the authorised conditions of use, the applicant submitted a tolerance study[18] and two literature searches.[19] However, the tolerance study was not further considered due to the absence of replication.

The two literature searches on the safety of Bonvital® covered eight databases: Agricola, Agris, Google Scholar, Ingenta, PubMed, Science Direct, Web of Science and World Cat Library for the period from 2006 to 2017. The search terms used were 'Bonvital' or '*Enterococcus faecium* DSM 7134' or 'DSM 7134' and 'piglets' or 'pigs for fattening' in one case, and 'Bonvital' or '*Enterococcus faecium* DSM 7134' and 'adverse effects' or 'interaction' or 'incompatibilities' or 'residues' or 'toxicological' or

[13] Technical dossier/Section II/Annex II.2-1.
[14] Technical dossier/Section II/Annexes II.2-2 and II.2-3.
[15] Technical dossier/Section II/Annex II.2-4.
[16] Technical dossier/Section II/Annex II.2-5.
[17] Technical dossier/Section II/Annex II.2-6.
[18] Technical dossiers/Section III/Annexes III.1
[19] Technical dossiers/Supplementary information February and March 2018/Annexes Supp info_2 and 3.

'epidemiological' or 'safety' or 'environment' or 'human' in the second case. A total of 16 publications fitted with the criteria of the first search; however, they concerned only efficacy trials (Appendix A). None of these papers reported any safety concern related to the supplementation of the additive to target species. The only relevant hit found in the second search was an EFSA opinion on the same product (EFSA, 2007a).

Considering the above, the FEEDAP Panel concludes that the additive remains safe under the authorised conditions of use.

The applicant proposed maximum use levels higher than the currently authorised (from 1×10^9 CFU/kg feed to 1×10^{10} CFU/kg feed in feed for piglets and from 1×10^9 CFU/kg feed to 2×10^9 CFU/kg feed in feed for pigs for fattening). Since neither the active agent nor the other components of the additive give rise to concerns, the conclusions reached before are considered to cover the higher maximum application rate proposed by the applicant.

Therefore, the Panel concludes that Bonvital® used under the proposed conditions of use is safe for weaned piglets and pigs for fattening, consumers of products derived from animals fed Bonvital® and the environment. Bonvital® is considered a potential skin and respiratory sensitiser.

3.3. Efficacy

In a previous opinion, Bonvital showed the potential to be efficacious at the minimum inclusion level of 1×10^9 CFU/kg feed in weaned piglets and at 5×10^8 CFU/kg feed in pigs for fattening (EFSA, 2007a). The minimum application rates proposed by the applicant already fall within the range of currently authorised for piglets and pigs for fattening, and therefore, the assessment of the efficacy would not be needed. Nonetheless, the applicant has provided some additional efficacy studies which are described below.

3.3.1. Efficacy for piglets

Four studies were submitted, three performed in the same Member State but in three different locations and one in a non-European country. This latter was the tolerance trial cited in Section 3.2, which cannot be further considered for the reasons explained above.[20]

The design of the studies is presented in Table 1 and the results in Table 2. In study 1,[21] weaned piglets were distributed based on weight and gender in four experimental groups: one receiving the basal unsupplemented diets, the second receiving the basal diets supplemented with Bonvital® providing 1×10^9 CFU/kg feed and the other two receiving different additives. Results obtained with the other additives were not considered by the working group. Studies 2[22] and 3[23] followed a similar design with two experimental groups; one receiving the basal unsupplemented diets and the second receiving the basal diets supplemented with Bonvital®. Study 1 included mixed-sex pens, study 3 single-sexed-pens, while in study 2, the sex was not specified, but the experiment included the same number of females and males. The diets were offered to the animals ad libitum and the intended cell counts were confirmed by analysis. Health status was monitored throughout the experimental periods. Individual (studies 1 and 3) or pen (study 2) weight and feed intake per pen were measured, and the feed to gain ratio per pen was calculated. In all studies, an analysis of variance (ANOVA) was performed with the data, including those from the relevant treatment groups only, considering as fixed effect the treatment group and as random effect the animal/pen. Since study 3 included four consecutive batches of piglets, batch and stable were also included as random factors. The pen was the experimental unit for all parameters.

[20] Technical dossier FAD-2016-0038/Section II/Annexes IV-1.
[21] Technical dossier FAD-2016-0038/Section II/Annexes IV-2/Supplementary information February 2018/Annexes Supp Info 4 and DK 1234 Raw data.
[22] Technical dossier FAD-2016-0038/Section II/Annexes IV-3/Supplementary information February 2018/Annex Supp Info 5.
[23] Technical dossier FAD-2016-0038/Section II/Annexes IV-4/Supplementary information February 2018/Annex Supp Info 6.

Table 1: Details on the study design for the studies performed in weaned piglets

Study	Breed (Age in days) (Sex)	Total animals Replicates/ treatment × animals/replicate	Duration of the study (days)	Basal diets (main ingredients) form
1	(Yorkshire × Landrace) × Duroc (25) 30♀, 40♂	70 7 × 5	42	Extruded maize/soybean meal/fish meal mash
2	Hybrids BHZP × (Large White × Landrace) (25) 14♀, 14♂	28 7 × 2	42	Maize/soybean meal, barley, wheat mash
3	BHZP (25) 189♀, 191♂	380 16 × 12(a)	47	Maize/soybean meal/wheat bran/fish meal mash

(a): Four pens contained 11 animals.

Table 2: Overview of results of efficacy studies with Bonvital® in weaned piglets

Study	Bonvital® (CFU/kg feed)	Initial weight (kg)	Final weight (kg)	Feed intake (g/d)	Average daily gain (g/d)	Feed to gain ratio	Mortality (n)
1	0	6.7	24.3	646	419[b]	1.54[a]	0
	1×10^9	6.7	25.7	641	451[a]	1.42[b]	0
2	0	7.3	26.9	691	466	1.49[a]	0
	1×10^9	7.3	27.6	676	483	1.40[b]	0
3	0	7.8	31.8	799	509	1.58[a]	1
	1×10^9	7.9	32.4	799	523	1.53[b]	1

[a,b]: Means in a column within a given trial with different superscript letters are significantly different $p \leq 0.05$.

Supplementation of the additive significantly improved the feed to gain ratio of animals in all studies.

The additional studies provided confirm the conclusions already expressed in the previous opinion (EFSA, 2007a) that Bonvital® has the potential to be efficacious in weaned piglets at 1×10^9 CFU/kg feed.

3.3.2. Efficacy for pigs for fattening

Three studies conducted in the same Member State but in two different locations were submitted. The design of the studies is presented in Table 3 and the results in Table 4. In all studies, animals were divided into pens in order to have a homogeneous distribution based on body weight and gender. Studies 1[24] and 3[25] involved single-sex pens while study 2[26] had mixed-sex pens. Pens were allocated to two experimental groups: one receiving the unsupplemented basal diets, and the second receiving the basal diets supplemented with the additive in order to provide 2×10^8 CFU/kg feed. Concentration in feed was confirmed by analysis. The animals were fed ad libitum. Pen feed intake was measured at the end of the feeding periods in study 1 and on a daily basis in studies 2 and 3. Pigs were individually weighed at the beginning and end of the trial and feed to gain ratio was calculated per pen. In study 3, all the pigs were killed at 116 kg body weight and the length of the fattening period was also subject to analysis. Morbidity and mortality were monitored in all studies. Growth data were analysed using an ANOVA with the fixed effect of the group and the random effect of the pen (for weight). Feed intake and feed to gain ratio were analysed with a linear model in study 1, and with t-test and U-test in studies 2 and 3. The experimental unit was the pen for all parameters.

[24] Technical dossier FAD-2016-0036/Section II/Annexes IV-1.
[25] Technical dossier FAD-2016-0036/Section II/Annexes IV-3 and Supplementary information March 2018/Annex Supp_Info 5.
[26] Technical dossier FAD-2016-0036/Section IV/Annexes IV-2 and Supplementary information March 2018/Annex Supp_Info 4.

Table 3: Details on the study design for the studies performed in pigs for fattening

Study	Breed Age in days (Sex)	Total animals Replicates/ treatment × animals/ replicate	Duration of the study (days)	Basal diets (main ingredients) form
1	DanBred × Pietrain 75 71♀, 72♂	143 36 × 2[(a)]	82	(Wheat, barley, rye, soybean meal) Mash
2	Unspecified 77 200♀, 200♂	400 8 × 25	91	(Wheat, barley, rye, soybean meal) Mash
3	Hybrids Hülsenberg 68 72♀, 72♂	144[(b)] 10/8[(c)] × 7/10	105/97[(d)]	(Wheat/triticale/soybean meal/barley) Not specified

(a): 1 pen of the control group with 1 animal.
(b): 76 in the control and 68 in Bonvital group.
(c): 10 pens in the control (2 pens of 10 animals and 8 of 7 animals) and 8 pens in the Bonvital group (4 pens of 10 animals and 4 pens of 7 animals).
(d): Duration was dictated by the slaughter weight of individual animals (average 105 days for the control and 97 days for the Bonvital group).

Table 4: Overview of results of efficacy studies with Bonvital® in pigs for fattening

Study	Bonvital® (CFU/kg feed)	Initial weight (kg)	Daily feed intake (kg/day)	Final weight (kg)	Average daily gain (g/d)	Feed:gain	Mortality and removals (n)
1	0 2×10^8	31.5[a] 28.3[b]	2.64 2.62	116 117	1026[b] 1083[a]	2.57[a] 2.42[b]	0 0
2	0 2×10^8	25.4 25.5	2.56 2.50	115 116	987 995	2.63[a] 2.55[b]	3 1
3	0 2×10^8	27.4 27.7	2.47[b] 2.58[a]	116[(1)] 116	851[b] 925[a]	2.98 2.88	1 0

[a,b]: Values within one column for the same study with different superscripts are different ($p < 0.05$).
(1): Final weight was reached at 105 days in the control group and at 97 days in the Bonvital® group.

Supplementation of the additive led to a significantly greater average daily gain in two trials (1 and 3) and a significantly better feed to gain ratio in one of these trials (study 1) and in the second trial (study 2). In study 3, the fattening period (to reach 116 kg) was also significantly reduced in the Bonvital® group (control: 105 vs Bonvital®: 97 days, $p = 0.029$).

Based on the new studies provided, the FEEDAP Panel concludes that Bonvital® has the potential to be efficacious in pigs for fattening at 2×10^8 CFU/kg feed.

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.

5. Conclusions

The applicant has provided evidence that the additive currently in the market complies with the conditions of authorisation.

The FEEDAP Panel concludes that the additive remains safe under the authorised conditions of use for the target animals, consumers, users and the environment. The higher inclusion rates proposed by the applicant are also considered safe. Therefore, the Panel concludes that Bonvital® used under the

[27] 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.

proposed conditions of use is safe for weaned piglets and pigs for fattening, consumers of products derived from animals fed Bonvital® and the environment. Bonvital® is considered a potential skin and respiratory sensitiser.

Bonvital® has the potential to be efficacious in weaned piglets at 1×10^9 CFU/kg feed and in pigs for fattening at 2×10^8 CFU/kg feed.

Documentation provided to EFSA

1) Bonvital – Pigs for fattening. June 2016. Submitted by Lactosan GmbH; Co. KG
2) Bonvital – Pigs for fattening. Supplementary information. March 2018. Submitted by Lactosan GmbH; Co. KG
3) Bonvital Piglets. June 2016. Submitted by Lactosan GmbH; Co. KG
4) Bonvital Piglets. Supplementary information. February 2018. Submitted by Lactosan GmbH; Co. KG
5) Comments from Member States.

Chronology EFSA-Q-2016-00452

Date	Event
3/6/2016	Dossier received by EFSA
6/7/2016	Reception mandate from the European Commission
5/10/2016	Application validated by EFSA – Start of the scientific assessment
10/10/2017	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation, safety for target species, safety for the consumer, safety for the user and efficacy*
5/1/2017	Comments received from Member States
26/2/2018	Reception of supplementary information from the applicant - Scientific assessment re-started
27/2/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

Chronology EFSA-Q-2016-00450

Date	Event
3/6/2016	Dossier received by EFSA
6/7/2016	Reception mandate from the European Commission
5/10/2016	Application validated by EFSA – Start of the scientific assessment
10/10/2017	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation and safety for target species, consumer, user and environment and efficacy*
5/1/2017	Comments received from Member States
15/3/2018	Reception of supplementary information from the applicant - Scientific assessment re-started
27/2/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ANOVA	analysis of variance
CFU	colony forming unit
EURL	European Union Reference Laboratory
LOQ	limit of quantification
MIC	minimum inhibitory concentration
PCR	polymerase chain reaction
PFGE	pulsed-field gel electrophoresis
RAPD	random amplification of polymorphic DNA

Appendix A – List of references retrieved from the literature search provided by the applicant to support safety of the additive

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