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

EFSA Panel on Additives and Products or Substances used in Animal Feed (EFSA FEEDAP Panel), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Maryline Kouba, Mojca Kos Durjava, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Villa, Ruud Woutersen, Andrew Chesson, Pier Sandro Cocconcelli, Guido Rychen, Robert John Wallace, Maria Saarela and Rosella Brozzi

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 $1 \times 10^9$ colony forming unit (CFU)/kg feed and in pigs for fattening at $2 \times 10^8$ CFU/kg feed.

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

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Correspondence: feedap@efsa.europa.eu
Panel members: Giovanna Azimonti, Vasileios Bampidis, Maria Bastos, Henrik Christensen, Birgit Dusemund, Maryline Kouba, Mojca Kos Durjava, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Villa and Ruud Woutersen.

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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\(^3\) (\textit{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 (\textit{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 \textit{Enterococcus faecium} (DSM 7134) and \textit{Lactobacillus rhamnosus} when used in feed for calves for rearing (EFSA FEEDAP Panel, 2013b).

Bonvital\(^4\) 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 \textit{E. faecium DSM 7134} is also authorised in combination with \textit{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 (\textit{Enterococcus faecium DSM 7134}) as a feed additive for weaned piglets and pigs for fattening.
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 429/200810 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 $1 \times 10^{10}$ 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 $1 \times 10^{10}$ 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).

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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.\(^\text{13}\) 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.\(^\text{14}\) RAPD and PFGE profiles were used to compare the active agent with the master cell bank culture.\(^\text{15}\) 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 IS16, *hyf*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).\(^\text{16}\) 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).\(^\text{17}\) 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 tolerability study\(^\text{18}\) and two literature searches.\(^\text{19}\) However, the tolerability 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

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\(^{13}\) 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 dossier/Section III/Annexes III.1
\(^{19}\) Technical dossier/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 \(1 \times 10^9\) CFU/kg feed to \(1 \times 10^{10}\) CFU/kg feed in feed for piglets and from \(1 \times 10^9\) CFU/kg feed to \(2 \times 10^9\) 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 sensitizer.

3.3. Efficacy

In a previous opinion, Bonvital showed the potential to be efficacious at the minimum inclusion level of \(1 \times 10^9\) CFU/kg feed in weaned piglets and at \(5 \times 10^8\) 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 \(1 \times 10^9\) 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.
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 $1 \times 10^9$ 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 and 2 involved single-sex pens while study 3 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 $2 \times 10^9$ 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. Mortality and morbidity 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.

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

| Study | Breed (Age in days) (Sex) | Total animals Replicates/treatment x animals/replicate | Duration of the study (days) | Basal diets (main ingredients) form |
|-------|---------------------------|-------------------------------------------------------|-----------------------------|-----------------------------------|
| 1     | (Yorkshire × Landrace) × Duroc (25) 30♀, 40♂ | 70 7 x 5 | 42 | Extruded maize/soybean meal/fish meal mash |
| 2     | Hybrids BHZP × (Large White × Landrace) (25) 14♀, 14♂ | 28 7 x 2 | 42 | Maize/soybean meal, barley, wheat mash |
| 3     | BHZP (25) 189♀, 191♂ | 380 16 x 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 | Initial weight (kg) | Final weight (kg) | Feed intake (g/d) | Average daily gain (g/d) | Feed to gain ratio | Mortality (n) |
|-------|---------------------|-------------------|-------------------|-------------------------|-------------------|---------------|
| 1     | 0 1 x 10⁹           | 6.7               | 24.3              | 646                     | 419b             | 1.54a         | 0             |
|       |                     | 6.7               | 25.7              | 641                     | 451b             | 1.42b         | 0             |
| 2     | 0 1 x 10⁹           | 7.3               | 26.9              | 691                     | 466              | 1.49a         | 0             |
|       |                     | 7.3               | 27.6              | 676                     | 483              | 1.40b         | 0             |
| 3     | 0 1 x 10⁹           | 7.8               | 31.8              | 799                     | 509              | 1.58a         | 1             |
|       |                     | 7.9               | 32.4              | 799                     | 523              | 1.53b         | 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 $1 \times 10^9$ CFU/kg feed.
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 \( 2 \times 10^8 \) 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

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\(^{27}\) 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 sensitizer.

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

**References**

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on a request from the Commission on the safety of product Bonvital (Provita E) for chickens for fattening. EFSA Journal 2004;2(11):120, 4 pp. [https://doi.org/10.2903/j.efsa.2004.120](https://doi.org/10.2903/j.efsa.2004.120)

EFSA (European Food Safety Authority), 2007a. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the safety and efficacy of product Bonvital, a preparation of Enterococcus faecium, as a feed additive for sows in accordance with Regulation (EC) No 1831/2003. EFSA Journal 2007;5(7):521, 8 pp. [https://doi.org/10.2903/j.efsa.2007.521](https://doi.org/10.2903/j.efsa.2007.521)

EFSA (European Food Safety Authority), 2007b. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the safety and efficacy of product Bonvital, a preparation of Enterococcus faecium, as a feed additive for pigs for fattening in accordance with Regulation (EC) No 1831/2003. EFSA Journal 2007;5(1):440, 9 pp. [https://doi.org/10.2903/j.efsa.2007.440](https://doi.org/10.2903/j.efsa.2007.440)
EFSA (European Food Safety Authority), 2009a. Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on a request from the European Commission on the safety and efficacy of Bonvital (Enterococcus faecium) as feed additive for chickens for fattening. EFSA Journal 2009;7 (3):990, 12 pp. https://doi.org/10.2903/j.efsa.2009.990

EFSA (European Food Safety Authority), 2009b. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific Opinion on of Bonvital as a feed additive for dogs. EFSA Journal 2009;7 (11):1379, 11 pp. https://doi.org/10.2903/j.efsa.2009.1379

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2010. Scientific Opinion on Bonvital (Enterococcus faecium) as a feed additive for chickens for fattening. EFSA Journal 2010;8 (6):1636, 5 pp. https://doi.org/10.2903/j.efsa.2010.1636

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), 2012a. 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), 2012b. Guidance on the assessment of bacterial susceptibility to antimicrobials of human and veterinary importance. EFSA Journal 2012;10(6):2740, 10 pp. https://doi.org/10.2903/j.efsa.2012.2740

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances Used in Animal Feed), 2012c. Guidance on the safety assessment of Enterococcus faecium in animal nutrition. EFSA Journal 2012;10(5):2682, 10 pp. https://doi.org/10.2903/j.efsa.2012.2682

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013a. Scientific Opinion on the safety and efficacy of Bonvital (Enterococcus faecium) for chickens reared for laying and minor avian species. EFSA Journal 2013;11(4):3167, 10 pp. https://doi.org/10.2903/j.efsa.2013.3167

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013b. Scientific Opinion on the safety and efficacy of Provita LE (Enterococcus faecium and Lactobacillus rhamnosus) as a feed additive for calves for rearing. EFSA Journal 2013;11(4):3175, 14 pp. https://doi.org/10.2903/j.efsa.2013.3175

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013c. Guidance on the renewal of the authorisation of feed additives. EFSA Journal 2013;11(10):3431, 8 pp. https://doi.org/10.2903/j.efsa.2013.3431

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2014. Scientific Opinion on the safety and efficacy of Bonvital (Enterococcus faecium) as a feed additive for sows. EFSA Journal 2014;12(2):3565, 9 pp. https://doi.org/10.2903/j.efsa.2014.3565

**Abbreviations**

ANNOVA 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

Bartkevičiūtė Z, Cernauskiénė J, Jeresiūnas, Kulys J, Jeroch H, 2005. Einfluss des Probiotikums Bonvital auf die Mast-und Schlachtleistung von Schweinen. BOKU-Symposium Tierernährung

Bindas L, Vajda V, Maskal’ová I, 2007. The effect of the probiotic Bonvital on production parameters in fattening pigs. Slovak agricultural university in Nitra, faculty of biotechnology and food sciences, department of animal physiology. VII. SLOVAK CONFERENCE OF ANIMAL PHYSIOLOGY, 23-24.5.2007

Branner GR, Roth-Maier DA, 2013. Influence of pre-, pro-, and synbiotics on the intestinal availability of different B-vitamins. Archived of Animal Nutrition, June 2006; 60(3): 191-204

Devi SM et Kim IH, 2014. Effect of medium chain fatty acids (MCFA) and probiotic (Enterococcus faecium) supplementation on the growth performance, digestibility and blood profiles in weaning pigs. Veterinarni Medicina, 59, 2014 (11): 527–535

EFSA (European Food Safety Authority), 2007a. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the safety and efficacy of product Bonvital, a preparation of Enterococcus faecium, as a feed additive for piglets and pigs for fattening in accordance with Regulation (EC) No 1831/2003. The EFSA Journal (2007) 440, 1-9

Gueimonde M, Frias R, Ouwehand AC, 2006. Assuring the continued safety of lactic acid bacteria used as probiotics. Biolegia, Bratislava, 61/6: 755—760, 2006, Section Cellular and Molecular Biology, https://doi.org/10.2478/s11756-006-0153-2

Horn L et Jeresiūnas A, 2006. Probiotinų ir mineralinių vitamininių papildų panaudojimas kiaulių šerime. Doctoral Thesis. LIETUVOS VETERINARIJOS AKADEMIJA GYVULININKYSTĖS TECHNOLOGIJOS FAKULTETAS GYVŪNŲ MITYBOS KATEDRA

Kwak W G, Park IH, Yun W, Lee JH, Lee CH, Oh SY, Oh HJ, Liu S, Kim YH, Park JC, Kim GS & Cho JH, 2017. Effects of various additives to enhance growth performance, blood profiles, and reduce malodour emissions in growing pigs. South African Journal of Animal Science 2017, 47 (No. 4)

Lojanica M, Manojlović M, Jeremić D, Petronijević S, 2010. The effects of probiotic Enterococcus faecium DSM 7134 in the weaned pigs nutrition. Biotechnology in Animal Husbandry 26 (1-2), p 57-64, 2010 ISSN 1450-9156

Roth-Maier A, Branner G (2006). Experimentelle Untersuchungen zur praecaecalen und faecalen Verdauung von prae- und symbiotischen Futterzusatzstoffen beim Schwein und deren Einfluss auf die Nährstoffverdaulichkeit und ausgewählte mikrobielle Parameter. Doctoral Thesis. Technische Universität München. Wissenschaftszentrum Weihenstephan für Ernährung, Landnutzung und Umwelt Department für Tierwissenschaften Fachgebiet Tierernährung

Shytaj F et Delia E, 2013. Using feed additives as a way to improve growth performance in weaned piglets. Albanian Journal of Agricultural Sciences;2013; 12 (4): 725-728

Shytaj F, Hajno L, Sula F, Delia E, 2014. The effect of combined preparation, probiotic and phytase on performance parameters and vitality of weaned piglets. Albanian Journal of Agricultural Sciences;2014 Special Issue, p. 277

Traknytė J et Bartkevičiūtė Z, 2006. Mineralinių vitamininių papildų, su biologiskai aktyvius medžiagomis, įtaka penimų kiaulių kai kuriems sveikatos, skerdenos ir mėsos kokybės rodikliams. Doctoral Thesis. LIETUVOS VETERINARIJOS AKADEMIJA GYVULININKYSTĖS TECHNOLOGIJOS FAKULTETAS GYVŪNŲ MITYBOS KATEDRA

Yan L et Kim IH, 2013. Effect of probiotics supplementation in diets with different nutrient densities on growth performance, nutrient digestibility, blood characteristics, faecal microbial population and faecal noxious gas content in growing pigs. Journal of Applied Animal Research, 41:1, 23-28, https://doi.org/10.1080/09712119.2012.739092

Zhang ZF et Kim IH, 2015. Effects of Enterococcus faecium DSM 7134 supplementation in different energy and crude protein density diets on ileal amino acid digestibility and intestinal shedding of lactobacilli and Escherichia coli in finishing pigs. Animal Feed Science and Technology 201 (2015) 115–119

Zhang ZF, Lee JM, Kim IH, 2014. Effects of Enterococcus faecium DSM 7134 on weanling pigs were influenced by dietary energy and crude protein density. Livestock Science 169 (2014) 106-111

Zhao PY, Tran HN, Shin HY, Kim IH, 2016. Effects of lactic acid bacteria complex and Enterococcus faecium DSM 7134 in weaning pigs. Journal of Animal Science, suppl. Supplement 2; Champaign Vol. 94, (Apr 2016):79