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Safety and efficacy of Biacton® (*Lactobacillus farciminis* CNCM I-3740) as a feed additive for weaned piglets

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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 Biacton® when used as a feed additive for weaned piglets. Biacton® is a preparation of viable cells of *Lactobacillus farciminis* CNCM I-3740 intended to be incorporated into feed for weaned piglets at a minimum recommended application level of 1×10^9 CFU/kg complete feed. *L. farciminis* is a species considered by EFSA to be suitable for the Qualified Presumption of Safety (QPS) approach to safety assessment which requires the identity of the strain to be conclusively established and evidence that it does not show acquired resistance to antibiotics of human and veterinary importance. The strain was found to meet the criteria for the QPS approach to safety assessment and since concerns are not expected from other components of the additive, the additive is presumed safe for all target species, consumers and the environment. Biacton® is not irritant to skin, eyes or to the respiratory tract, but should be considered a prespiratory sensitiser. In the absence of data, no conclusions could be drawn on the potential skin sensitisation potential of the additive. No conclusion can be drawn on the efficacy of Biacton® for weaned piglets based on the data available.

Keywords: zootechnical additive, other zootechnical additives, Biacton®, *Lactobacillus farciminis* CNCM I-3740, Safety, QPS, efficacy

Requestor: European Commission

Question number: EFSA-Q-2016-00712

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

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 INNOFI S.A.[2] for authorisation of Biacton® (*Lactobacillus farciminis* CNCM I-3740[3]), when used as a feed additive for weaned piglets (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). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 31 July 2017.

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 Biacton (*Lactobacillus farciminis* CNCM I-3740), when used under the proposed conditions of use (see Section 3.2).

1.2. Additional information

Biacton® is a preparation of viable cells of *Lactobacillus farciminis* CNCM I-3740. EFSA adopted on opinion on the safety of Biacton® for chickens for fattening, turkeys and laying hens for use as a feed additive in accordance with Council Directive 70/524/EEC (EFSA, 2006).

Biacton® is currently authorised for chickens for fattening, turkeys and laying hens.[4]

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[5] in support of the authorisation request for the use of Biacton as a feed additive.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the active agent in animal feed. The Executive Summary of the EURL report can be found in Annex A.[6]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Biacton® is in line with the principles laid down in Regulation (EC) No 429/2008[7] and the relevant guidance documents: Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011), Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012a), and Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b) and Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018).

[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] INNOFI SA 1 rue Pierre et Marie Curie, 22190, Plerin, France.
[3] Formerly identified as *Lactobacillus farciminis* CNCM MA 67/4R.
[4] Commission Regulation (EC) No 1876/2006 of 18 December 2006 concerning the provisional and permanent authorisation of certain additives in feedingstuffs. OJ L 360, 19.12.2006, p. 16 plus amendments.
[5] FEED dossier reference: FAD-2016-0048.
[6] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/finrep_fad-2016-0024_lactobacillus_farciminis.pdf
[7] 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

The additive Biacton® is a preparation of viable cells of *L. farciminis* CNCM I-3740 intended to be used as a zootechnical additive (functional group: gut flora stabilisers) in feed for weaned piglets to improve performance.

3.1. Characterisation

3.1.1. Characterisation of the active agent

The strain of *L. farciminis* was isolated from a healthy pig and is deposited [redacted] Identity was established by whole genome sequence (WGS) analysis. [redacted]

The susceptibility of the strain to the antibiotics recommended [redacted] Exceedance of the cut-off value by one dilution is considered to be within the normal range of variation and thus, not a matter of concern.

[redacted] The analysis performed did not identify any hit of concern. [redacted] do not raise safety concerns.

3.1.2. Characterisation of the additive

The active agent is produced by batch fermentation with a medium typical for the commercial production of lactic acid bacteria (details provided). [redacted]

Three batches of the additive were analysed for the presence chemical contaminants.[13] Results showed values below the detection limits (mercury and arsenic < 0.005 mg/kg additive, aflatoxin B1 < 0.001 mg/kg additive) or values that do not raise concerns (lead ≤ 0.16 mg/kg additive). Three batches were analysed for microbiological contamination.[14] [redacted] were compliant with the specifications.

[redacted]

[13] Technical dossier/Section II/Annex II.1_214.
[14] Technical dossier/Section II/Annex II.1_214 [redacted]

[redacted]

3.1.3. Stability and homogeneity

The stability [redacted] was tested [redacted]

To investigate the capacity of the additive ([redacted]) to be homogeneously distribute into a feed [redacted]

3.2. Conditions of use

The additive is intended to be incorporated into feed for weaned piglets, either directly of via a premixture, at a minimum recommended application level of 1×10^9 CFU/kg complete feed.

3.3. Safety

3.3.1. Safety for the target species, consumers and environment

The bacterial species *L. farciminis* is considered by EFSA to be potentially suitable for the qualified presumption of safety (QPS) approach to safety assessment (EFSA, 2007; EFSA BIOHAZ Panel, 2020). This approach requires the identity of the strain to be conclusively established and evidence that the it does not harbour acquired antimicrobial genes to clinically relevant antibiotics. In the view of the FEEDAP Panel, the antibiotic resistance qualification has been met and the identity of the strain established as *L. farciminis*. Therefore, *L. farciminis* CNCM I-3740 is considered by EFSA to be suitable for the QPS approach to safety assessment and, consequently, is presumed safe for the target species, consumers of products from animals fed the additive and the environment. Since no concerns arise from other components of the additive, Biacton® is also presumed safe for the target animals, consumers and the environment.

3.3.2. Safety for the user

Dermal[21] and eye[22] irritation tests were performed following the OECD guidelines 404 and 405, respectively. No cutaneous reactions were observed in the dermal irritation test while in the eye irritation test only transient and slight conjunctival reactions were observed. Consequently, it is concluded that the additive is non-irritant to eyes and skin.

No test of skin sensitisation was reported.

[redacted]

[21] Technical dossier/Section III/Annex III.7_3312b.
[22] Technical dossier/Section III/Annex III.6_3312a.

An acute inhalation toxicity test was conducted following the OECD Guideline 403.[23] Rats were exposed to an aerosol of *L. farciminis* cells for a single 4-h period. Health and behaviour were monitored for 14 days and then all rats were killed and subjected to a gross pathological examination. No evidence of respiratory irritation or systemic toxicity was observed.

Since a significant fraction of the additive consists of inhalable particles, and its active agent is of proteinaceous nature, Biacton® should be considered a respiratory sensitiser.

3.4. Efficacy

Four trials are presented, three made in Europe and the fourth in an extra-EU country. However, three studies could not be further considered due to flaws in the design and reporting. In particular, short duration (i.e. 35 days and not reaching a daily weight gain of at least 500 g) and poor reporting (e.g. no mortality data) in one study,[24]

Therefore, in the absence of evidence, the FEEDAP Panel cannot conclude on the efficacy of Biacton® for weaned piglets.

3.5. 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[32] and Good Manufacturing Practice.

[23] Technical dossier/Section III/Annex III.5_3311.
[24] Technical dossier/Section IV/Annexes IV.2_222 and IV.5_222.
[26] Technical dossier/Section IV/Annexes IV.3_223 and IV.6_223/
[30] Technical dossier/Section IV/Annexes IV.1_221 and IV.4_221
[32] 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.

4. Conclusions

The active agent fulfils the requirements of the QPS approach to the assessment of safety and no concerns are expected from other components of the additive. Consequently, Biacton® can be presumed to be safe for the target animals, consumers of products from treated animals and the environment.

Biacton® is not irritant to skin, eyes or the respiratory tract, but should be considered a respiratory sensitiser. In the absence of data, no conclusions could be drawn on the skin sensitisation potential of the additive.

No conclusion can be drawn on the efficacy of Biacton® for weaned piglets based on the data available.

5. Documentation as provided to EFSA/Chronology

Date	Event
04/05/2017	Dossier received by EFSA. Additive for piglets. Submitted by INNOFI S.A
06/06/2017	Reception mandate from the European Commission
18/07/2017	Application validated by EFSA – Start of the scientific assessment
13/09/2017	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: safety for the consumer*
29/09/2017	Reception of supplementary information from the applicant - Scientific assessment re-started
19/10/2017	Comments received from Member States
18/11/2017	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
13/03/2018	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*
13/11/2018	Reception of supplementary information from the applicant - Scientific assessment re-started
20/12/2018	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*
26/02/2019	Reception of supplementary information from the applicant - Scientific assessment re-started
03/02/2020	Reception of spontaneous supplementary information from the applicant
19/03/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

CFU	colony forming unit
EURL	European Union Reference Laboratory
MIC	minimum inhibitory concentration
OECD	Organisation for Economic Co-operation and Development
PFGE	pulsed field gel electrophoresis
QPS	Qualified Presumption of Safety
WGS	whole genome sequence

Annex A – Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Biacton

In the current application authorisation is sought under Article 4(1) for *Lactobacillus farciminis* (CNCM MA 67/4R[33]) under the category/functional group 4(b) 'zootechnical additives'/'gut flora stabilisers', according to Annex I of Regulation (EC) No 1831/2003. Authorisation is sought for the use of the *feed additive* for piglets (weaned). This *feed additive* is already authorised for other animal species by Regulation (EC) No 1876/2006.

According to the Applicant, the feed additive contains as active substance *Lactobacillus farciminis* (CNCM MA 67/4R). The *feed additive* is to be marketed with a minimum *Lactobacillus farciminis* (CNCM MA 67/4R) content of 10^9 Colony Forming Unit (CFU)/g. It is intended to be incorporated through premixtures at a minimum content of 10^9 CFU/kg *feedingstuffs*.

For the identification of *Lactobacillus farciminis* (CNCM MA 67/4R) the Applicant applied partial 16S rDNA gene sequence analysis. The EURL recommends instead for official control Pulsed Field Gel Electrophoresis (PFGE), a generally recognised methodology for genetic identification of bacterial strains.

For the enumeration of *Lactobacillus farciminis* (CNCM MA 67/4R) in the *feed additive* and *feedingstuffs*, the Applicant applied an amended French Standard (NF V04-503, 1988). The EURL recommends instead for official control the ring-trial validated spread plate method EN 15787.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.

[33] Now renamed as *L. farciminis* CNCM I-3740.