

ADOPTED: 17 January 2023

doi: 10.2903/j.efsa.2023.7818

Modification of the conditions of the authorisation of *Clostridium butyricum* FERM BP-2789 (Miya-Gold®) for chickens for fattening, chickens reared for laying and minor avian species (excluding laying birds) (Miyarisan Pharmaceutical Co. Ltd)

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Abstract

The additive Miya-Gold® consists of viable cells of *Clostridium butyricum* FERM BP-2789. The additive is currently authorised in the EU for use as a feed additive for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), piglets (suckling and weaned) and piglets of minor porcine species. The authorisation for chickens and minor poultry species for fattening and reared for laying is at a minimum level of 2.5×10^8 CFU/kg complete feed. The applicant has requested to lower this level to 1.25×10^8 CFU/kg feed. The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) did not consider any of the five long-term trials and one pooled analysis of two of them as supporting evidence for the efficacy of the additive at the lower dose due to the incompliance of the husbandry conditions in which the chickens were reared with those indicated in Directive 2007/43/EC. Owing to the lack of adequate data, the Panel is not in the position to conclude on the efficacy of Miya-Gold® at 1.25×10^8 CFU/kg feed for the target species.

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Keywords: zootechnical additives, gut flora stabiliser, efficacy, poultry, Miya-Gold®

Requestor: European Commission

Question number: EFSA-Q-2021-00384

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Declarations of interest: If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

Acknowledgements: The Panel wishes to thank the following for the support provided to this scientific output (in alphabetical order of the last name): Daniel Plaza, Barbara Rossi and the FEEDAP Working Group on Animal Nutrition.

Suggested citation: 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, Durjava M, Kouba M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Brozzi R, Pettenati E, Revez J, Anguita M, Galobart J and Ortuño J, 2023. Scientific Opinion on the modification of the conditions of the authorisation of *Clostridium butyricum* FERM BP-2789 (Miya-Gold®) for chickens for fattening, chickens reared for laying and minor avian species (excluding laying birds) (Miyarisan Pharmaceutical Co. Ltd). EFSA Journal 2023;21(2):7818, 7 pp. <https://doi.org/10.2903/j.efsa.2023.7818>

ISSN: 1831-4732

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The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.



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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States.

The European Commission received a request from Miyarisan Pharmaceutical Co. Ltd represented in the European Union (EU) by Huvepharma NV Belgium² for the modification of the terms of the authorisation of the additive consisting of *Clostridium butyricum* FERM BP-2789 (Miya-Gold[®]), when used as a feed additive for chickens and minor poultry species for fattening and reared for laying (category: zootechnical additive; 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 13(3) (modification of the authorisation of a feed additive). The particulars and documents in support of the application were considered valid by EFSA as of 14 February 2022.

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 feed additive consisting of *Clostridium butyricum* FERM BP-2789 (Miya-Gold[®]), when used under the proposed conditions of use (see Section 3.1).

1.2. Additional information

The additive is based on viable spores of *C. butyricum* FERM BP-2789.

EFSA has issued five opinions on the safety and efficacy of the additive based on *C. butyricum* FERM BP-2789: one for chickens for fattening (EFSA, 2009); one for weaned piglets, weaned minor porcine species and minor avian species (EFSA FEEDAP Panel, 2011); one for chickens for fattening, chickens reared for laying and minor avian species (EFSA FEEDAP Panel, 2013); one for turkeys for fattening and turkeys reared for breeding (EFSA FEEDAP Panel, 2014); and, the most recent one, for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), piglets (suckling and weaned) and minor porcine species opinion (EFSA FEEDAP Panel, 2021).

The additive is currently authorised for use in feed for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), piglets (suckling and weaned) and piglets of minor porcine species (4b1830).³

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁴ in support of the authorisation request for the use of *C. butyricum* FERM BP-2789 (Miya-Gold[®]) as a feed additive.

¹ Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

² Miyarisan Pharmaceutical Co. Ltd represented in EU by Huvepharma NV Belgium, Uitbreidingstraat 80, B-2600, Berchem (Antwerpen) Belgium

³ COMMISSION IMPLEMENTING REGULATION (EU) 2021/1411 of 27 August 2021 concerning the renewal of the authorisation of *Clostridium butyricum* FERM BP-2789 as a feed additive for chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), weaned piglets and weaned minor porcine species, its authorisation for chickens for fattening, suckling piglets and suckling minor porcine species, and repealing Implementing Regulations (EU) No 373/2011, (EU) No 374/2013 and (EU) No 1108/2014 (holder of authorisation Miyarisan Pharmaceutical Co. Ltd represented by Huvepharma NV Belgium).

⁴ FEED dossier reference: FEED-2021-0402.

In accordance with Article 38 of the Regulation (EC) No 178/2002⁵ and taking into account the protection of confidential information and of personal data in accordance with Articles 39 to 39 e of the same Regulation, and of the Decision of EFSA's Executive Director laying down practical arrangements concerning transparency and confidentiality,⁶ a non-confidential version of the dossier has been published on Open.EFSA.⁷

According to Article 32c(2) of Regulation (EC) No 178/2002 and to the Decision of EFSA's Executive Director laying down the practical arrangements on pre-submission phase and public consultations,⁸ EFSA carried out a public consultation on the non-confidential version of the application from 28 November to 19 December 2022. Two entries were registered but the comments submitted dimmed as not relevant to the scope of the public consultation, and therefore, were not considered further.

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

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment regarding the methods used for the control of the *C. butyricum* in animal feed are valid and applicable for the current application.⁹

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of *Clostridium butyricum* FERM BP-2789 (Miya-Gold[®]) is in line with the principles laid down in Regulation (EC) No 429/2008¹⁰ and the relevant guidance documents: Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017) and Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

3. Assessment

The additive consisting of *C. butyricum* FERM BP-2789, hereafter referred to by its trade name Miya-Gold[®], is authorised in the EU as a zotechnical additive (functional group: gut flora stabilisers) to be used in feed for chickens for fattening, chickens reared for laying, minor avian species (excluding laying birds), piglets (suckling and weaned) and piglets of minor porcine species at a minimum use level of 2.5×10^8 CFU/kg complete feed; and in turkeys for fattening and reared for breeding, at a minimum use level of 1.25×10^8 CFU/kg complete feed.

The present application is for the modification of the current authorisation to reduce the minimum use level in chickens for fattening, chickens reared for laying and minor avian species (excluding laying birds) from 2.5×10^8 CFU/kg to 1.25×10^8 CFU/kg complete feed.

3.1. Characterisation and conditions of use

The additive Miya-Gold[®] is based on the spores of *C. butyricum* FERM BP-2789. The identity of the active agent, its lack of toxigenic potential and its susceptibility to the relevant antibiotics were established in a previous opinion in which the additive was fully characterised (EFSA FEEDAP Panel, 2021). The additive is authorised in solid form at a concentration of at least 5×10^8 CFU/g. Compliance with this specification was demonstrated in five recent batches of Miya-Gold[®] (average content of 5.5×10^8 (range 5.0–6.5) CFU/g).¹¹

No other new information has been submitted with regards to the identity and characterisation of the additive and the Panel considers that the information previously assessed applies to the current assessment.

⁵ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p.1–48.

⁶ Decision available at: <https://www.efsa.europa.eu/en/corporate-pubs/transparency-regulation-practical-arrangements>

⁷ Available at: <https://open.efsa.europa.eu/dossier/FEED-2021-0402>

⁸ Decision available at: https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/210111-PAs-pre-submission-phase-and-public-consultations.pdf

⁹ The full report is available on the EU Science Hub website: <https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2008-0012.pdf> and <https://joint-research-centre.ec.europa.eu/system/files/2013-02/FinRep-FAD-2010-0005.pdf>

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 Annex_II_1_3_1_recent_batch_variation.

The additive Miya-Gold[®] is currently authorised for use in feed for chickens for fattening and reared for laying, minor avian species (excluding laying birds), weaned piglets and weaned minor porcine species at a minimum recommended inclusion level of 2.5×10^8 CFU/kg complete feed and in turkeys for fattening and turkeys reared for breeding at a minimum recommended inclusion level of 1.25×10^8 CFU/kg complete feed.

The applicant has requested to modify these conditions of use by reducing the minimum recommended inclusion level in chickens for fattening and reared for laying and minor avian species (excluding laying birds) to 1.25×10^8 CFU/kg complete feed.

3.2. Safety

Safety aspects regarding the use of Miya-Gold[®] in feed including the safety for the target animals, consumers, users and the environment have been evaluated in previous opinions (EFSA, 2009; EFSA FEEDAP Panel, 2011, 2013, 2014, 2021). In the most recent opinion, the Panel concluded that the additive Miya-Gold[®] is safe for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), piglets (suckling and weaned) and piglets of minor porcine species, the consumer and the environment under the currently authorised conditions of use. Regarding the safety for the user, the Panel concluded that the additive is not irritant to skin and eyes and that sensitisation via respiratory route cannot be excluded.

The FEEDAP Panel is not aware of any new information that would lead it to reconsider the conclusions drawn previously. The reduction in the recommended use level in chickens for fattening and other minor poultry species does not have an impact on the safety aspects already considered.

3.3. Efficacy

A total of five trials in chickens for fattening and a pooled study (resulting from the pooling of two of the trials provided) were submitted.¹² However, none of the studies were further considered as the husbandry conditions in which the birds were kept during the *in vivo* trials were not in line with Directive 2007/43/EC¹³ (mainly regarding the bedding used).

Owing to the lack of adequate data, the FEEDAP Panel is not in the position to conclude on the efficacy of Miya-Gold[®] at 1.25×10^8 CFU/kg complete feed for chickens for fattening, and, consequently, for any other minor avian species.

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 Regulation¹⁴ and Good Manufacturing Practice.

4. Conclusions

The additive is safe for the target species, the consumer and the environment under the current authorised conditions of use. Regarding the safety for the user, the additive is not irritant to skin and eyes and sensitisation via respiratory route cannot be excluded. The proposed modification to the conditions of the authorisation does not have an impact on the safety conclusions previously established.

Owing to the lack of adequate data, the FEEDAP Panel is not in the position to conclude on the efficacy of Miya-Gold[®] at 1.25×10^8 CFU/kg complete feed for chickens for fattening, and, consequently, to extend or extrapolate the efficacy to other minor avian categories and species.

¹² Annex_IV_3_1; Annex_IV_3_2; Annex_IV_3_3; Annex_IV_3_4; Annex_IV_3_5; Annex_IV_3_6.

¹³ Council Directive 2007/43/EC of 28 June 2007 laying down minimum rules for the protection of chickens kept for meat production, OJ L 182 12.7.2007, p. 19.

¹⁴ Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

5. Documentation provided to EFSA/Chronology

Date	Event
29/07/2021	Dossier received by EFSA. Miya-Gold [®] (Preparation of <i>Clostridium butyricum</i> FERM BP-2789). Submitted by Miyarisan Pharmaceutical Co. Ltd (represented in the European Union (EU) by Huvepharma NV Belgium)
08/10/2021	Reception mandate from the European Commission
14/02/2022	Application validated by EFSA – Start of the scientific assessment
27/05/2022	Comments received from Member States
19/12/2022	Comments received from Public Consultation
17/01/2023	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

- EFSA (European Food Safety Authority), 2009. 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 the product Miya-Gold[®]S (*Clostridium butyricum*) as a feed additive for chickens for fattening. EFSA Journal 2009;7(4):1039, 16 pp. <https://doi.org/10.2903/j.efsa.2009.1039>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011. Scientific Opinion on Miya-Gold[®] (*Clostridium butyricum*) as a feed additive for weaned piglets, minor weaned porcine species and minor avian species. EFSA Journal 2011;9(1):1951, 15 pp. <https://doi.org/10.2903/j.efsa.2011.1951>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013. Scientific Opinion on the safety and efficacy of Miya-Gold[®] (*Clostridium butyricum*) for chickens for fattening, chickens reared for laying and minor avian species. EFSA Journal 2013;11(1):3040, 9 pp. <https://doi.org/10.2903/j.efsa.2013.3040>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2014. Scientific Opinion on the safety and efficacy of Miya-Gold[®] (*Clostridium butyricum*) for turkeys for fattening and turkeys reared for breeding. EFSA Journal 2014;12(3):3603, 10 pp. <https://doi.org/10.2903/j.efsa.2014.3603>
- 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 and Innocenti ML, 2017. Guidance on the identity, characterisation and conditions of use of feed additives. EFSA Journal 2017;15(10):5023, 12 pp. <https://doi.org/10.2903/j.efsa.2017.5023>
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- 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, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Cocconcelli PS, Glandorf B, Herman L, Maradona MP, Saarela M, Anguita M, Galobart J, Holczknecht O, Manini P, Pizzo F, Tarrés-Call J and Pettenati E, 2021. Scientific Opinion on the safety and efficacy of the feed additive consisting of *Clostridium butyricum* FERM BP-2789 (Miya-Gold[®]S) for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding, minor avian species (excluding laying birds), piglets (suckling and weaned) and minor porcine species. EFSA Journal 2021;19(3):6450, 11 pp. <https://doi.org/10.2903/j.efsa.2021.6450>

Abbreviations

CFU	colony forming unit
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed