

ADOPTED: 5 July 2018

doi: 10.2903/j.efsa.2018.5385

## Assessment of the application for renewal of authorisation of Levucell<sup>®</sup> SC (*Saccharomyces cerevisiae* CNCM I-1077) as a feed additive for dairy ewes and dairy goats

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### Abstract

Levucell<sup>®</sup> SC is the trade name for a feed additive based on viable cells of a strain *Saccharomyces cerevisiae*. The product is currently authorised for use in feed for horses, lambs, dairy sheep, dairy goats, dairy cows and cattle for fattening. This opinion concerns the renewal of the authorisation of Levucell<sup>®</sup> SC as a zootechnical additive for dairy ewes and dairy goats. *S. cerevisiae* is considered by EFSA to be suitable for the Qualified Presumption of Safety (QPS) approach to establishing safety for the target species, consumers and the environment. The identity of the strain present in the additive was established. Accordingly, this strain is presumed safe for the target species, consumers of products from animals fed the additive and the environment. Since no concerns are expected from other components of the additive, Levucell<sup>®</sup> SC is considered safe for the target species, consumers of products from animals fed the additive and the environment. The applicant has provided data demonstrating that the additive currently in the market complies with the conditions of authorisation. Furthermore, according to the information provided in the technical dossier, no new evidence has been identified that would make the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) reconsider the previous conclusions on the safety of the product for target species, consumers and the environment under the authorised conditions of use.

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**Keywords:** zootechnical additives, Levucell<sup>®</sup> SC, *Saccharomyces cerevisiae* CNCM I-1077, safety, QPS, ewes, goats

**Requestor:** European Commission

**Question number:** EFSA-Q-2016-00298

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**Acknowledgements:** The EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed) wishes to thank the following for the support provided to this scientific output: Jaume Galobart, Lucilla Gregoret, Orsolya Holczknecht and Paola Manini.

**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, Kouba M, Kos Durjava M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa R, Woutersen R, Chesson A, Coconcelli PS, Wallace RJ, Rychen G, Brozzi R and Saarela M, 2018. Scientific Opinion on the assessment of the application for renewal of authorisation of Levucell® SC (*Saccharomyces cerevisiae* CNCM I-1077) as a feed additive for dairy ewes and dairy goats. *EFSA Journal* 2018;16(7):5385, 12 pp. <https://doi.org/10.2903/j.efsa.2018.5385>

**ISSN:** 1831-4732

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



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## 1. Introduction

### 1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003<sup>1</sup> 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 a request from Lallemand SAS<sup>2</sup> for renewal of the authorisation of the product Levucell® SC (*Saccharomyces cerevisiae* CNCM I-1077), when used as a feed additive for dairy ewes and dairy goats (category: zootechnical additive; functional groups: gut flora stabiliser).

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 14(1) (renewal of an authorised 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 1 June 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 Levucell® SC (*Saccharomyces cerevisiae* CNCM I-1077), when used under the proposed conditions of use (see Section 3.1.3).

### 1.2. Interpretation of the Terms of Reference

The application for renewal of the authorisation does not include a proposal for amending or supplementing the conditions of the original authorisation that would have an impact on the efficacy of the additive; therefore, efficacy is not assessed. The present opinion will focus only on the safety aspects.

### 1.3. Additional information

The Scientific Committee on Animal Nutrition (SCAN) issued an opinion on the safety of this product for beef and dairy cattle, including the safety for the user, the consumer and the environment (European Commission, 1997/2003). EFSA issued several opinions on the safety and efficacy of this product for dairy goats and dairy ewes (EFSA, 2006a), leisure horses (EFSA, 2006b, 2009), lambs for fattening (EFSA, 2008) and dairy cows, cattle for fattening, minor ruminant species and camelids (EFSA FEEDAP Panel, 2017).

The product is currently authorised for use in horses,<sup>3</sup> lambs,<sup>4</sup> dairy sheep, dairy goats,<sup>5</sup> dairy cows and cattle for fattening.<sup>6</sup>

## 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<sup>7</sup> in support of the request for the renewal of the authorisation for the use of Levucell® SC (*Saccharomyces cerevisiae* CNCM I-1077) as a feed additive. The technical dossier was prepared

<sup>1</sup> 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.

<sup>2</sup> Lallemand SAS. 137, 19 Rue des Briquetiers, BP 31702. 59700 Blagnac, France.

<sup>3</sup> Commission Regulation (EC) No 910/2009 of 29 September 2009 concerning the authorisation of a new use of the preparation of *Saccharomyces cerevisiae* CNCM I-1077 as a feed additive for horses (holder of authorisation Lallemand SAS). OJ L 257, 30.9.2009, p. 7.

<sup>4</sup> Commission Regulation (EC) No 1293/2008 of 18 December 2008 concerning the authorisation of a new use of *Saccharomyces cerevisiae* CNCM I-1077 (Levucell SC20 and Levucell SC10 ME) as a feed additive. OJ L 340, 19.12.2008, p. 38, plus amendments.

<sup>5</sup> Commission Regulation (EC) No 226/2007 of 1 March 2007 concerning the authorisation of *Saccharomyces cerevisiae* CNCM I 1077 (Levucell SC20 and Levucell SC10 ME) as a feed additive. OJ L 64, 2.3.2007, p. 26, plus amendments.

<sup>6</sup> Commission Regulation (EC) No 1200/2005 of 26 July 2005 concerning the permanent authorisation of certain additives in feedingstuffs and the provisional authorisation of a new use of an additive already authorised in feedingstuffs. OJ L 195, 27.7.2005, p. 6, plus amendments.

<sup>7</sup> FEED dossier reference: FAD-2016-0024.

following the provisions of Article 7 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008 and the applicable EFSA guidance documents.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessments are valid and applicable for the current application.<sup>8</sup>

## 2.2. Methodologies

The approach followed by the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) to assess the safety and the efficacy of Levucell® SC (*Saccharomyces cerevisiae* CNCM I-1077) is in line with the principles laid down in Regulation (EC) No 429/2008<sup>9</sup> and the relevant guidance documents: Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013).

## 3. Assessment

The additive Levucell® SC is a preparation consisting of dried cells of *Saccharomyces cerevisiae* CNCM I-1077, with no excipients, intended for use as a zootechnical additive (gut flora stabiliser) in feed for dairy goats and dairy ewes.

### 3.1. Characterisation

#### 3.1.1. Characterisation of the additive

The product is authorised in two forms:

- Levucell® SC20<sup>10</sup>, a fine, granulated free-flowing powder with a minimum concentration of viable yeast cells of  $2 \times 10^{10}$  colony forming units (CFU)/g of additive (granulated form),
- Levucell® SC10 ME<sup>11</sup>, with a minimum concentration of viable yeast cells of  $1 \times 10^{10}$  CFU/g of additive (coated or microencapsulated form).

The applicant is requesting the authorisation of a third form, Levucell® SC ME Titan<sup>12</sup>, [REDACTED].<sup>13</sup> For practical purposes, the two coated forms are considered equivalent.

The applicant states that no changes in the manufacturing process or composition of the additive have been introduced since the authorisation (other than the production of the SC10ME Titan form, see above). This was confirmed by the analysis of three batches of each form produced in 2015, which showed compliance with specifications ( $2.7 \times 10^{10}$ – $2.9 \times 10^{10}$  CFU/g for SC20;  $1.5 \times 10^{10}$ – $1.8 \times 10^{10}$  CFU/g for SC10 ME;  $1.3 \times 10^{10}$ – $2.3 \times 10^{10}$  CFU/g for SC10 ME Titan).<sup>14</sup>

Microbiological purity was also confirmed by the analysis of three production batches of each form of the additive produced in 2015. Measurements for the SC20 form included aerobic bacteria ( $1.6 \times 10^3$ – $2.6 \times 10^3$  CFU/g), total coliforms ( $< 10^3$  CFU/g), *Escherichia coli* (absent), *Staphylococcus* (absent) and *Salmonella* (absence in 25 g).<sup>15</sup> For the other forms, values were provided for enterobacteria ( $< 10^3$  CFU/g), *E. coli* ( $< 10$  CFU/g), *Staphylococcus* ( $< 10$  CFU/g) and *Salmonella* (absence in 25 g).<sup>16</sup>

<sup>8</sup> The reports linked to the previous dossiers are available on the EURL website: <https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports/fad-2005-0016?search&form-return> and <https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports/fad-2010-0120?search&form-return>

<sup>9</sup> 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.

<sup>10</sup> Levucell® SC20 may be marketed with other tradenames: Levupro SC20/SC10 ME/SC10 ME Titan.

<sup>11</sup> Levucell® SC10 ME may be marketed with other tradenames: Proficell SC20/SC10 ME/SC10 ME Titan.

<sup>12</sup> Levucell® SC Titan may be marketed with other tradenames: Lallemand SC20/SC10 ME/SC10 ME Titan.

<sup>13</sup> The applicant claims that 'the Standing Committee on the Food Chain and Animal Health in its meeting of 18 February 2010 concluded that Levucell® SC ME Titan falls within the description as provided for in the authorisation Regulation'.

<sup>14</sup> Technical dossier/Section II/Annex II 3a to Annex II 3c.

<sup>15</sup> Technical dossier/Section II/Annex II 3a.

<sup>16</sup> Technical dossier/Section II/Annex II 3b and 3c.

Chemical contamination was measured in three 2015 batches of the SC20<sup>17</sup> and SC10 ME Titan<sup>18</sup> forms. Data were provided for heavy metals (cadmium < 0.05 mg/kg, mercury ≤ 0.12 mg/kg, lead < 0.2 mg/kg), arsenic (< 0.2 mg/kg); mycotoxins (aflatoxin B1 < 0.1 µg/kg, aflatoxin B2 (only for SC20) < 1.0 µg/kg, aflatoxin G1 (only for SC20) < 1.0 µg/kg, aflatoxin G2 (only for SC20) < 1.0 µg/kg, ochratoxin A < 0.25 µg/kg and zearalenone < 10 µg/kg); dioxins (≤ 0.28 pg/kg) and dioxin-like polychlorinated biphenyls (PCBs, only for SC20, ≤ 0.04 pg/kg). For the SC10 ME form, data on three batches from 2014 were provided, showing similar values.<sup>19</sup> Although the batches dated from more than one year prior to the submission, given that the product is obtained downstream from the SC20 form, they are considered acceptable.

### 3.1.2. Characterisation of the active agent

The active agent is a *S. cerevisiae* strain deposited at the National Culture Collection of Microorganisms (CNCM, France) with the accession number CNCM I-1077.<sup>20</sup> [REDACTED]

### 3.1.3. Conditions of use

Levucell® SC20 and Levucell® SC10 ME are currently authorised at a minimum level of  $1.2 \times 10^9$  CFU/kg of complete feed for dairy sheep and  $5 \times 10^8$  CFU/kg of complete feed for dairy goats, with no maximum level. The applicant proposes to keep these conditions.

Under other provisions the regulation foresees that storage temperature, storage life and stability to pelleting be indicated in the directions for use of the additive and premixtures.

## 3.2. Safety

### 3.2.1. Safety for the target species, consumers and the environment

The species *S. cerevisiae* is considered by EFSA to be suitable for the Qualified Presumption of Safety (QPS) approach to safety assessment (EFSA, 2007, EFSA BIOHAZ Panel, 2017). This approach requires the identity of the strain to be conclusively established. In the view of the FEEDAP Panel, the identity of the active agent was confirmed as *S. cerevisiae*. Accordingly, it is considered by EFSA to be suitable for the QPS approach to safety and is presumed safe for the target species, consumers of products from animals fed the additive and the environment. Since no concerns are expected from other components of the additive, Levucell® SC is considered safe for the target species, consumers of products from animals fed the additive and the environment.

### 3.2.2. Safety for the user

In a previous opinion, the FEEDAP Panel concluded that Levucell® SC is not a skin irritant or sensitiser but is an eye irritant. Inhalation exposure is unlikely. Encapsulation is not expected to introduce hazards for users (EFSA FEEDAP Panel, 2017).

### 3.2.3. Further evidence of safety

The applicant states that no adverse effects or specific interactions or incompatibilities have been reported for the additive.<sup>22</sup>

The applicant conducted a literature search on the safety of Levucell® SC using several databases: CAB Abstracts, Agris, Scopus, Google Scholar, Bielefeld Academic Search Engine (BASE) and the Liège University library.<sup>23</sup> The search included the terms: CNCM I-1077, Levucell SC, *Saccharomyces cerevisiae*, safe\*, tox\*, tolerance, adverse effects, epidemiology, feed, incompatib\* and interact\*. The search covered the period 2006–2018. The search identified 74 relevant publications (Appendix A). None was designed to assess the safety *per se* of the additive, but the effects of Levucell® SC on the

<sup>17</sup> Technical dossier/Section II/Annex II 4a and 4b.

<sup>18</sup> Technical dossier/Section II/Annex II 4d and 4e.

<sup>19</sup> Technical dossier/Section II/Annex II 4c.

<sup>20</sup> Technical dossier/Section II/Annex II 6b.

<sup>22</sup> Technical dossier/Section III.

<sup>23</sup> Technical dossier/Supplementary information March 2018.



performance of animals. However, some studies investigated or included some health end-points (i.e. blood biochemistry). None of these studies reported safety issues with the additive under assessment.

Therefore, the FEEDAP Panel concludes that there is no new evidence that would lead the Panel to reconsider its previous conclusions on the safety of the product for target species, consumers and the environment under the authorised conditions of use.

### 3.3. 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<sup>24</sup> and Good Manufacturing Practice.

## 4. Conclusions

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

The FEEDAP Panel confirms its previous conclusion that Levucell® SC is safe for the target species, consumers of products from animals fed the additive, users and the environment.

### Documentation provided to EFSA

- 1) Levucell SC. *Saccharomyces cerevisiae* CNCM I-1077 for dairy goats and dairy ewes. March 2016. Submitted by Lallemand SAS.
- 2) Application for renewal of the authorisation of *Saccharomyces cerevisiae* CNCM I-1077 (Levucell SC) for dairy goats and dairy ewes under Article 14 of Regulation (EC) No 1831/2003. Supplementary Information. March 2018. Submitted by Lallemand SAS.

### Chronology

Date	Event
23/3/2016	Dossier received by EFSA
14/4/2016	Reception mandate from the European Commission
1/6/2016	Application validated by EFSA – Start of the scientific assessment
15/12/2017	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: safety for target species, consumer, user and environment</i>
1/9/2016	Comments received from Member States
10/2/2016	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
22/3/2018	Reception of supplementary information from the applicant – Scientific assessment re-started
5/7/2018	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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<sup>24</sup> Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 January 2003 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

- EFSA (European Food Safety Authority), 2008. 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 Levucell SC20/Levucell SC10ME, a preparation of *Saccharomyces cerevisiae*, as feed additive for lambs for fattening. EFSA Journal 2008;772, 1–11.
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- EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Girones R, Herman L, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Ru G, Sanaa M, Simmons M, Skandamis P, Snary E, Speybroeck N, Ter Kuile B, Threlfall J, Wahlström H, Cocconcelli PS, Klein G (deceased), Prieto Maradona M, Querol A, Peixe L, Suarez JE, Sundh I, Vlak JM, Aguilera-Gomez M, Barizzone F, Brozzi R, Correia S, Heng L, Istace F, Lythgo C and Fernández Escámez PS, 2017. Scientific Opinion on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA. EFSA Journal 2017;15(3):4664, 177 pp. <https://doi.org/10.2903/j.efsa.2017.4664>
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## Abbreviations

BIOHAZ	EFSA Panel on Biological Hazards
CFU	colonyforming unit
EURL	European Union Reference Laboratory
FEEDAP	EFSA Panel on additives and products or substances used in animal feed
PCBs	polychlorinated biphenyls
PCR	polymerase chain reaction
QPS	Qualified Presumption of Safety
SCAN	Scientific Committee on Animal Nutrition



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

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