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Assessment of the application for renewal of authorisation of Yea-Sacc[®] (*Saccharomyces cerevisiae*) for horses

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Abstract

Yea-Sacc[®] is an additive based on a live preparation of a strain of *Saccharomyces cerevisiae* intended for use as a zootechnical additive (digestibility enhancer). The current assessment is performed in the context of the renewal of the authorisation of the feed additive; however, the applicant proposed also to lower (6.5×10^8 colony forming unit (CFU)/kg of complete feedingstuff) the minimum dose of the additive when used in feed for horses. The additive is produced in a powder (Yea-Sacc[®]) and in a prills (Yea-Sacc[®]_TS) forms. The Panel considered that the additive currently on the market complies with the existing conditions of authorisation. *Saccharomyces cerevisiae* is considered by EFSA to be suitable for the qualified presumption of safety approach to safety assessment. As the identity of the production strain has been confirmed, safety for the target species, consumer and the environment were presumed. Both formulations are non-irritant to skin, Yea-Sacc[®]_TS is non-irritant to the eye while Yea-Sacc[®] is a moderate irritant. Both formulations should be considered skin sensitisers and because of their high proteinaceous nature, they should be considered as potential respiratory sensitisers. The applicant submitted two efficacy studies: the FEEDAP Panel concluded that in the first study inconsistent results were observed for the two lower doses which are considered microbiologically equivalent. The second study demonstrated that Yea-Sacc[®] at the level of 7.5×10^8 resulted in a better digestion of organic matter which may be explained by increases in digestibility of the fibre. Based on the data provided, the FEEDAP Panel cannot conclude on the efficacy of Yea-sacc[®] when used as a feed additive in horses at the proposed level (6.5×10^8 CFU/kg complete feed).

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1. Introduction

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

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest one year before the expiry date of the authorisation.

The European Commission received a request from Alltech Ireland² for renewal of the authorisation of the product Yea-Sacc® (*Saccharomyces cerevisiae* CBS 493.94), when used as a feed additive for horses (category: zootechnical additive; functional group: digestibility enhancer).

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 the authorisation). The particulars and documents in support of the application were considered valid by EFSA as of 19 December 2018.

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 Yea-Sacc® (*Saccharomyces cerevisiae* CBS 493.94) when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

Yea-Sacc® is the trade name of an additive based on a preparation of a strain of yeast (*Saccharomyces cerevisiae* CBS 493.94).

The product is currently authorised for use in horses,³ dairy cows and minor dairy ruminant species, cattle for fattening and minor ruminant species for fattening.⁴

EFSA published three opinions on the product Yea-Sacc®: one on the safety for leisure horses (EFSA, 2003), one on the safety and efficacy of the same product for horses (EFSA, 2009) and another one on the safety and efficacy of Yea-Sacc® when used in cattle for fattening, goats for fattening, dairy cows, dairy sheep, dairy goats and buffaloes (EFSA FEEDAP Panel, 2014).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁵ in support of the authorisation request for the use of Yea-Sacc® (*Saccharomyces cerevisiae* CBS 493.94) as a feed additive.

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

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.⁶

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Yea-Sacc® (*Saccharomyces cerevisiae* CBS 493.94) is in line with the principles laid down in Regulation (EC)

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 Alltech Ireland, Sarney, Summerhill Road, Dunboyne, Co. Meath, A86 X006, Ireland.

³ Regulation (EC) No 886/2009 of 25 September 2009 concerning the authorisation of the preparation of *Saccharomyces cerevisiae* CBS 493.94 as a feed additive for horses (holder of authorisation Alltech France). OJ L 254, 26.9.2009, p. 2.

⁴ Commission implementing Regulation (EC) No 1109/2014 of 20 October 2014 concerning the authorisation of the preparation of *Saccharomyces cerevisiae* CBS 493.94 as a feed additive for cattle for fattening, minor ruminant species for fattening, dairy cows and minor dairy ruminant species and amending Regulations (EC) No 1288/2004 and (EC) No 1811/2005 (holder of authorisation Alltech France). OJ L 301, 21.10.2014, p. 3.

⁵ FEED dossier reference: FAD-2018-0072.

⁶ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2007-0048.pdf>

No 429/2008⁷ and the relevant guidance documents: Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018a) and Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b).

3. Assessment

The additive Yea-Sacc® is a preparation of a strain of yeast (*Saccharomyces cerevisiae* CBS 493.94), intended for use as a zootechnical additive (functional group: digestibility enhancer) in feed for horses. The current assessment is performed in the context of the renewal of the authorisation of the feed additive. The applicant is also proposing to lower the minimum dose of the additive when used in feed for horses.

3.1. Characterisation

3.1.1. Characterisation of the active agent

The active agent is a *S. cerevisiae* strain which is deposited both in the National Collection of Yeast Cultures (UK) with a designation NCYC 1026 and the Centraalbureau voor Schimmelcultures (NL) with the accession number CBS 493.94.⁸

The whole genome of *S. cerevisiae* CBS 493.94 was sequenced and its taxonomic identification was confirmed by comparison of the D2 region of the LSU rRNA gene sequence with sequences from the validated MicroSEQ library.⁹ The sequence showed 100% similarity with *S. cerevisiae*. Moreover, the whole genome sequence (WGS) of the active agent was interrogated for the presence of antimicrobial resistance (AMR) genes and virulence factors. The presence of AMR genes was investigated comparing the sequence to the Comprehensive Antibiotic Resistance Database (CARD) and the presence of virulence factors was investigated by comparing the sequence to the Virulence Factors of Pathogenic Bacteria (VFDB) database. No known genes coding for antimicrobial resistance or virulence factors were found in the genome of the active agent.

3.1.2. Characterisation of the additive

The feed additive is marketed in two forms: dry powder (Yea-Sacc®) and prills (Yea-Sacc®_TS).

No changes in the manufacturing process or in the composition of the additive were proposed by the applicant. This was confirmed by the analysis of five batches of the additive in prills form produced in 2017–2018, and from the analysis of five batches of the additive in powder form produced in 2018–2019, which showed compliance with the current specifications for the additive (solid form minimum of 1×10^9 colony forming unit (CFU)/g additive).

Microbiological purity was also confirmed by the analysis of five batches of Yea-Sacc®_TS in prills produced in 2017–2018. Measurements for Yea-Sacc®_TS in prills included *Escherichia coli* (< 10 CFU/g), Sulfite-Reducing Anaerobes (< 10 CFU/g), *Salmonella* (absent), coagulase-positive staphylococci (< 1,000 CFU/g), *Listeria monocytogenes* (absent/25 g), *Clostridium perfringens* (< 10 CFU/g), moulds (< 10 CFU/g), coliforms (< 10 CFU/g). In addition, the applicant provided analytical results on the possible presence of mycotoxins (aflatoxin B1, zearalenone, ochratoxin A, fumonisin (B1 + B2), deoxynivalenol, T2 toxin and HT-2 toxin) and heavy metals: lead (0.014 mg/kg), cadmium (0.016 mg/kg), mercury (0.007 mg/kg). Results on concentration of arsenic (0.257 mg/kg) were also provided by the applicant. All the results were below the limits established by relevant EU Directive (2002/32 EC). The amount of the impurities in the product does not raise a safety concern.

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.

⁸ Technical dossier/Section II/Annex II_2_3.

⁹ Technical dossier/Section II/Supplementary information/Annex II_2_1, 2_2,2_3,2_4, 2_5.

3.1.3. Stability and homogeneity

3.1.3.1. Shelf-life of the additive

A new study on four batches of Yea-Sacc®_TS stored at 25°C (relative humidity (RH) 60%), for 12 months has been provided by the applicant. The data demonstrated that no significant losses of the content of *Saccharomyces cerevisiae* CBS 493.9 were observed.¹⁰

3.1.3.2. Homogeneity

The applicant provided homogeneity distribution data on Yea-Sacc®_TS in an equine feed.

The base mixture was made of barley, wheat, wheat bran, soybean meal and alfalfa pellets. The target yeast inclusion level was 1.39×10^7 CFU/g. This premixture was then added to the base mixture in the twin shaft mixer and mixed for 2 minutes. From this mixture, ten 200 g samples were taken to determine the homogenous distribution of the yeast preparation. The coefficient of variation (CV) was 80.94%. The analysis showed wide variation (6.0×10^5 – 3×10^7 CFU/g).¹¹

3.1.4. Conditions of use

The feed additive is currently authorised for feed for horses at a minimum content of 1.6×10^9 CFU/kg complete feed. The applicant is now asking to reduce the minimum content to 6.5×10^8 CFU/kg of complete feed.

3.2. Safety

Saccharomyces cerevisiae was considered by EFSA to be suitable for the qualified presumption of safety approach to safety assessment. As the identity of the production strain was established and as the additive essentially consists only of the active agent, safety for the target species, consumer and the environment were presumed (EFSA FEEDAP Panel, 2014).

In the present application, the applicant has provided up to date confirmation of the taxonomical identification of the strain as *S. cerevisiae*. Consequently, the additive can be presumed as safe for the target species, the consumer and the environment.

The safety for the user was evaluated by EFSA FEEDAP Panel in previous assessment (EFSA FEEDAP Panel, 2014). The FEEDAP Panel concluded that both formulations are non-irritant to skin, Yea-Sacc®_TS is non-irritant to the eye while Yea-Sacc® is a moderate irritant. Due to lack of data, both formulations should be considered skin sensitisers and because of their high proteinaceous nature, they should be considered as potential respiratory sensitisers. Yea-Sacc®_TS is designed to reduce dustiness and no significant exposure of users is to be expected for this form. In the absence of data on the dusting potential of Yea-Sacc®, it would be prudent to treat it as a respiratory sensitiser.

3.3. Efficacy

The applicant is asking to lower the minimum dose of the feed additive from 1.6×10^9 to 6.5×10^8 CFU/kg feed. In support of this modification, the applicant submitted two efficacy studies conducted on horses.

3.3.1. Efficacy for horses

Trial I



¹⁰ Technical dossier/Section II/Annex II_4_3.

¹¹ Technical dossier/Section II/Annex II_4_12.

[REDACTED]

Results are presented in Table 1.

Table 1: Effects of Yea-sacc® on the faecal apparent digestibility in horses (trial I)

| [REDACTED] |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| [REDACTED] |
| [REDACTED] |
| [REDACTED] |

[REDACTED]

[REDACTED]

Trial II

[REDACTED]

Results are presented in Table 2.

Table 2: Effects of Yea-sacc® on the faecal apparent digestibility in horses (trial II)

| [REDACTED] |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| [REDACTED] |
| [REDACTED] |

[REDACTED]

[REDACTED]

3.3.2. Conclusions on efficacy

The FEEDAP Panel concluded that in the first study inconsistent results were observed for the two lower doses which are considered microbiologically equivalent. Moreover, a significant effect was reported only for hemicellulose which was not considered sufficient by the Panel.

The second study demonstrated that Yea-Sacc at the level of 7.5×10^8 resulted in a better digestion of organic matter which may be explained by increases in digestibility of the fibre.

Based on the data provided, the FEEDAP Panel cannot conclude on the efficacy of Yea-sacc® when used as a feed additive in horses at the proposed level (6.5×10^8 CFU/kg complete feed).

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 currently on the market complies with the existing conditions of authorisation. The FEEDAP Panel concludes that Yea-sacc® remains safe for horses, consumers of products from animals fed the additive and the environment under the approved conditions of authorisation. Both formulations are non-irritant to skin, Yea-Sacc®_TS is non-irritant to the eye while Yea-Sacc® is a moderate irritant. Both formulations should be considered skin sensitisers and because of their high proteinaceous nature, they should be considered as potential respiratory sensitisers. The FEEDAP Panel cannot conclude on the efficacy of Yea-sacc® when used as a feed additive in horses at the proposed use level.

5. Documentation as provided to EFSA/Chronology

Date	Event
16/10/2018	Dossier received by EFSA. Yea-Sacc® - <i>Saccharomyces cerevisiae</i> CBS 493.94. Submitted by Alltech Ireland
07/11/2018	Reception mandate from the European Commission
19/12/2018	Application validated by EFSA – Start of the scientific assessment
21/12/2018	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: efficacy</i>
30/04/2019	Reception of supplementary information from the applicant - Scientific assessment re-started
19/03/2019	Comments received from Member States
12/11/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

- EFSA (European Food Safety Authority), 2003. Opinion of the Scientific Panel on additives and products or substances used in animal feed on the safety of the product Yea-Sacc® for leisure horses. EFSA Journal 2003;2(3):7, 5 pp. <https://doi.org/10.2903/j.efsa.2003.7>
- EFSA (European Food Safety Authority), 2009. Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the safety and efficacy Yea-Sacc1026® (*Saccharomyces cerevisiae*) for horses. EFSA Journal 2009;7(3):991, 15 pp. <https://doi.org/10.2903/j.efsa.2009.991>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013. 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>

¹⁴ Regulation (EC) No 1831/2005 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.

- EFSA FEEDAP Panel (EFSA Panel on Products or Substances used in Animal Feed), 2014. Scientific opinion on the safety and efficacy of Yea-Sacc® (*Saccharomyces cerevisiae*) as a feed additive for cattle for fattening, goats for fattening, dairy cows, dairy sheep, dairy goats and buffaloes. EFSA Journal 2014;12(5):3666, 15 pp. <https://doi.org/10.2903/j.efsa.2014.3666>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018a. Guidance on the characterisation of microorganisms used as feed additives or as production organisms. EFSA Journal 2018;16(3):5206, 24 pp. <https://doi.org/10.2903/j.efsa.2018.5206>
- EFSA FEEDAP Panel (EFSA Panel on additives and products or substances used in animal feed), 2018b. Guidance on the assessment of the efficacy of feed additives. EFSA Journal 2018;16(5):5274, 25 pp. <https://doi.org/10.2903/j.efsa.2018.5274>

Abbreviations

ADF	acid detergent fibre
AMR	antimicrobial resistance
bw	body weight
CARD	Antibiotic Resistance Database
CF	crude fibre
CFU	colony forming unit
CV	coefficient of variation
DM	dry matter
EURL	European Union Reference Laboratory
NDF	neutral detergent fibre
OM	organic matter
PCR	polymerase Chain Reaction
RH	relative humidity
VFDB	Virulence Factors of Pathogenic Bacteria database
WGS	whole genome sequence