Safety Assessment: Outcome of assessment of Selenised yeast *Saccharomyces cerevisiae* CNCM I-3060 inactivated, as a feed additive for all animal species

Reference number RP222

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Regulated Product Dossier Assessment

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Summary

An application was submitted to the Food Standards Agency (FSA) in February 2021 from All-technology Ireland Ltd. (Alltech Ireland), ("the applicant") for the authorisation of an additive containing selenised inactivated *Saccharomyces cerevisiae* CNCM I-3060. The application is for a modification of authorisation, in the category of 'nutritional additives', functional group 'compound of trace elements', as a source of selenium for feed. The modification proposed to increase the maximum dose of selenium content from 2000 mg Se/kg to 3500 mg Se/kg.

To support the FSA and Food Standards Scotland (FSS) in evaluating the dossier, the Animal Feed and Feed Additives Joint Expert Group (AFFAJEG) and the Advisory Committee on Animal Feedingstuffs (ACAF) were asked to review the dossier and the supplementary information from the applicant. ACAF concluded that the additive can be considered safe for the target species, the consumer and the environment as long as the limits of 0.2 mg Se/kg (supplementation) and 0.5 mg Se/kg (total feed) are not exceeded. The AFFAJEG concluded that the additive should be considered as hazardous through inhalation, as well as a respiratory sensitiser, and to not be a skin sensitiser, skin irritant or eye irritant.

No demonstration of efficacy was required for the renewal of authorisation.

The views of AFFAJEG and ACAF have been taken into account in the safety assessment which represents the opinion of the FSA and FSS.

1. Introduction

The FSA and FSS have undertaken a risk assessment for a feed additive (*Saccharomyces cerevisiae* CNCM I-3060 (Sel-Plex®), Sarney, Summerhill Road, Dunboyne, County Meath, Ireland) containing a maximum of 0.2 mg Se/kg in complete feed, under Regulation (EC) No 1831/2003[1] under the category of 'nutritional additives', functional group 'compound of trace elements. To support the safety assessment by FSA and FSS, the AFFAJEG and the ACAF provided advice to the FSA and FSS outlined in this document.

The dossier was evaluated on behalf of the FSA and FSS by the AFFAJEG. In line with Article 8 of 1831/2003, the assessment has considered whether the feed additive complies with the conditions laid down in Article 5, including: safety considerations for human, animal and environmental health; efficacy of the additive for its intended effect; potential impairment of the distinctive features of animal products This, and the guidance put in place by EFSA for the evaluation of feed additive applications, has formed the basis and structure for the assessment.

With thanks to the members of the AFFAJEG and ACAF during the course of the assessment, who were: Professor John Wallace, Professor Nicholas Jonsson, Martin Briggs, Dr. Katrina Campbell, Susan MacDonald, Professor Matthew Fisher, Christine McAlinden, Dr. Donald Morrison, Derek Renshaw, Dr. Michael Salter, Dr. Adam Smith and Dr. Nick Wheelhouse. Dr. Helen Warren declared a conflict of interest for the application and did not take part in the assessment.

The dossier was evaluated by the AFFAJEG at their October 2021 and December 2021 meetings. Further information was provided by the applicant in November 2021 responding to queries by AFFAJEG. The conclusions by the AFFAJEG were reviewed and approved by the ACAF, at their October 2022 meeting.

This document outlines the discussion and conclusions of the AFFAJEG's assessment on the safety and efficacy of Selenised yeast *Saccharomyces cerevisiae* CNCM I-3060 (inactivated) as a feed additive.

To refer to the additive under assessment, the proposed trade name (Sel-Plex) will be used throughout the rest of the document.

2. Assessment

2.1. Section II: Identity, characterisation and conditions of use

The additive is a preparation of organic selenium (97-99%) produced by *Saccharomyces cerevisiae*, composed mainly of selenomethionine (63%) and low molecular weight selenocomponents (34-36%). Data from several batches supporting the specification values was provided by the applicant:

Table 1: Identity table Sel-Plex®

Composition	
Organic selenium	97-99%
Selenomethionine	63% of total selenium
Low molecular weight selenocomponents	32-36% of total selenium
Chemical-physical specifications	
Density	1.328 g/cm^3
Dusting potential Particle size distribution	1,255 - 2,240 mg/m^3 Averages of: < 1µm = 0.13%; < 10 µm = 4.03%; < 50 µm = 56.59%; < 100 µm = 91.34%
Microbiological profile (CFU/g)	
Salmonella	Absent
Listeria monocytogenes	Absent
Coliforms	<10 CFU/g
Escherichia coli	<10 CFU/g
Staphylococcus aureus	<10 CFU/g
Anaerobic sulphite reducers	<10 CFU/g
Clostridium perfringens	<10 CFU/g
Yeasts and moulds	<10 CFU/g
Heavy metals	
Arsenic	0.388 mg/kg
Lead	0.077 mg/kg
Cadmium	0.022 mg/kg
Mercury	0.007 mg/kg

The FSA requested clarification from the applicant on whether the selenocomponents' behaviour was expected to be different to the main active principle, and whether these differences would impact the safety of the additive at the higher maximum dose proposed. The applicant provided an extensive response regarding the safety of the selenocomponents based on existing information from scientific literature, EFSA documentation and existing data from commercial companies. The AFFAJEG concluded that the selenocomponents were not an additional cause for safety concerns.

The additive is manufactured according to the process used for baker's yeast to produce yeast biomass, through which the mineral source of selenium is transformed into the organic form. *Saccharomyces cerevisiae* is a qualified presumption of safety (QPS) organism. The application presented a whole genome sequence (WGS) analysis and evidence of absence of the microorganism or its DNA in the final product, in line with guidance recommendations. The AFFAJEG evaluated the WGS data and determined that the microorganism used as active substance of the additive is identical to the QPS registered microorganism, that it is not capable of producing antimicrobial substances and therefore is free from any antibiotic activity. The microorganism does not carry antimicrobial resistance genes. No further concerns were raised by the Group.

The additive is proposed to be used as shown in the following table:

Table 2: Proposed mode of use of Sel-Plex® as described in the application

Proposed mode of use in animal nutrition			
Additive		Selenised yeast *S. cerevisiae* CNCM I-3060 inactivated	
Registration number/EC No/No		3b810	
Category(-ies) of additive		Nutritional	
Functional group(s) of additive		Compound of trace elements	
Description			
Composition, description		**Purity criteria**	**Method of analysis**
Preparation of selenised yeast		Containing: 2000 to 3500 mg Se/kg	I.S. EN 16159: Hydride generation atomic absorption spectrometry
Trade name (if appropriate)			Sel-Plex
Name of the holder of authorisation (if appropriate)			--
Conditions of use			
Species or category of animal	**Maximum Age**	**Minimum content**	**Maximum content**
		Amount of selenium in complete feed (12% moisture)	
All animal species	--	--	0.2 mg Se/kg

2.1.1. Conclusions on Section II

No further concerns were raised for Section II of the application dossier.

2.2. Section III: Safety

2.2.1. Safety for the target species

The applicant presented evidence of safety for the target species through previous conclusions from EFSA which stated that the additive is safe for the target species respecting the maximum total selenium dosage of 0.5 mg Se/kg[2,3,4,5,6,7]. The Joint Expert Group discussed the evidence presented and the possibility that the proposed increase in the maximum concentration of the additive to 3500 mg Se/kg could result in exceeding the total 0.5 mg Se/kg limit in feed (including supplementation and base feed selenium levels). It was concluded that, since the average concentration of the additive is 3074 +/- 55 mg Se/kg (mean +/- standard deviation), it would be very unlikely that the total 0.5 mg Se/kg limit would be exceeded.

The Group also questioned whether selenomethionine would have as narrow a margin of safety as inorganic selenium has when used as a supplement. It was concluded that, although selenomethionine has a higher deposition rate than inorganic selenium, it can be considered as safe for the target species, as long as the 0.2 mg Se/kg of

supplementation is not exceeded. Overall, the AFFAJEG concluded that based on the information presented, the additive remains safe for the target species after the modification of authorisation.

2.2.2. Safety for the consumer

The applicant presented evidence of safety for the consumer in the form of an EFSA opinion for the renewal of authorisation of the additive in 2018[8]. The AFFAJEG evaluated the data and the information provided by the applicant on the safety of selenocomponents of the additive, and concluded that the additive remains safe for consumers, as long as the 0.2 mg Se/kg limit of supplementation and the total 0.5 mg Se/kg limit of selenium in feed are not exceeded.

2.2.3. Safety for the user/worker

The applicant provided data from an acute dermal irritation/corrosion test following OECD 404, and an acute eye irritation test following OECD 405. The AFFAJEG concluded that based on the data presented and previous EFSA opinions the additive could be considered to be non-irritant to eyes and skin, and to not be a skin sensitiser. The AFFAJEG noted that the dusting potential of the additive was significantly high, above the 1000 mg/m^3 limit considered to be of concern, as well as a high concentration of particles of less than 50 µm diameter, indicating that workers could be exposed to a respirable dust when handling the additive. Based on the proteinaceous nature of the microorganism, the AFFAJEG concluded that the additive should be considered a respiratory sensitiser and hazardous through inhalation and recommended that safety precautions be taken to limit exposure of workers to inhalation of dust from the additive.

The AFFAJEG concluded that the additive is a respiratory sensitiser, and that the additive is not a skin sensitiser or a skin or eye irritant.

2.2.4. Safety for the environment

The applicant provided conclusions from previous EFSA assessments on the safety for the environment[8]. The AFFAJEG evaluated the data and concluded that the additive can be considered safe for the environment, as long as the limits of 0.2 mg Se/kg (supplementation) and 0.5 mg Se/kg (total feed) are not exceeded.

2.2.5. Conclusions on safety

The AFFAJEG concluded that the additive can be considered safe for the target species, the consumer and the environment as long as the limits of 0.2 mg Se/kg (supplementation) and 0.5 mg Se/kg (total feed) are not exceeded.

The additive should be considered as hazardous through inhalation, as well as a respiratory sensitiser, and to not be a skin sensitiser, skin irritant or eye irritant.

2.3. Section IV: Efficacy

For the modification of authorisation, no demonstration of efficacy was required. The AFFAJEG concluded the additive remains efficacious for all animal species.

3. Analytical methods evaluation

Conclusions on the analytical methods are presented here as an extract from the Evaluation Report of the European Union Reference Laboratory for Feed Additives (EURL-FA) on the Method(s) of the Analysis for Sel-Plex® 10^9:

For the determination of selenomethionine in the feed additive the applicant proposed a triple proteolytic digestion/extraction followed by anion-exchange high performance chromatography coupled to inductively coupled plasma mass spectrometry (HPLC-ICPMS). The European Union Reference Laboratory (EURL) recommends for official control the single laboratory validated and further verified HPLC-ICPMS method submitted by the applicant.

For the determination of total selenium in the feed additive, premixtures and feedingstuffs, the applicants proposed a microwave digestion using nitric acid and hydrogen peroxide followed by inductively coupled plasma mass spectrometry (ICPMS). The EURL recommends for official control the single laboratory validated and further verified ICPMS method submitted by the applicant to determine total selenium in the feed additive. However, for the determination of total selenium in feedingstuffs and premixtures, the EURL recommends the ring trial validated CEN method (prEN 16159:2010) for official control.

Further testing or validation of the methods is not considered necessary.

FSA/FSS accept the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Conclusions

The data presented in the application identified and characterised the additive adequately.

Data provided, together with evidence from previous EFSA opinions are sufficient evidence to demonstrate the safety of the additive for the target species, consumers and the environment as long as the limits of 0.2 mg Se/kg (supplementation) and 0.5 mg Se/kg (total feed) are not exceeded. The additive should be considered as hazardous through inhalation, as well as a respiratory sensitiser, and to not be a skin sensitiser, skin irritant or eye irritant.

No demonstration of efficacy was required for the modification of authorisation.

FSA/FSS accept the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

5. References

1. EC (European Commission), 2003. Regulation No 1831/2993 of the European Parliament and of the Council on additives for use in animal nutrition.

2. EFSA (European Food Safety Authority), 2006. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the safety and efficacy of the product Selenium enriched yeast (Saccharomyces cerevisiae NCYC R397) as a feed additive for all species in accordance with Regulation (EC) No 1831/2003. EFSA Journal 2007, 5(1):430, 23. DOI: 10.2903/j.efsa.2007.430

3. EFSA (European Food Safety Authority), 2009. Safety and efficacy of SELSAF (Selenium enriched yeast from Saccharomyces cerevisiae CNCM I-3399) as feed additive for all species. EFSA Journal 2009, 992, 124. DOI: 10.2903/j.efsa.2009.992

4. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2011a. Scientific Opinion on the safety and efficacy of selenium in the form of organic compounds produced by the selenium-enriched yeast Saccharomyces cerevisiae NCYC R645 (SelenoSource AF 2000) for all species. EFSA Journal 2011, 9(6):2279, 15. DOI: 10.2903/j.efsa.2011.2279

5. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2011b. Scientific Opinion on Safety and efficacy of Sel-Plex® (organic form of selenium produced by Saccharomyces cerevisiae CNCM I-3060) for all species. EFSA Journal 2011, 9(4):2110, 52. DOI: 10.2903/j.efsa.2011.2110

6. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2012. Scientific Opinion on safety and efficacy of selenium in the form of organic compounds produced by the selenium-enriched yeast Saccharomyces cerevisiae NCYC R646 (Selemax 1000/2000) as feed additive for all species. EFSA Journal 2012, 10(7):2778, 17. DOI: 10.2903/j.efsa.2012.2778

7. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2014. Scientific Opinion on the safety and efficacy of DL-selenomethionine as a feed additive for all animal species. EFSA Journal 2014, 12(2):3567, 20. DOI: 10.2903/j.efsa.2014.3567

8. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2018. Assessment of the application for renewal of authorisation of selenomethionine produced by Saccharomyces cerevisiae CNCM I-3060 (selenised yeast inactivated) for all animal species EFSA Journal 2018;16(7):5386, 14 pp. https://doi.org/10.2903/j.efsa.2018.5386

9. EURL-FA (European Reference Laboratory for Feed Additives), 2009. Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003. Selenomethionine.

6. Abbreviations

- FSA Food Standards Agency
- FSS Food Standards Scotland
- ACAF Advisory Committee on Animal Feedingstuffs
- AFFAJEG Joint Expert Group On Animal Feed And Feed Additives
- EFSA European Food Safety Authority
- QPS Qualified Presumption of Safety
- WGS Whole genome sequence
- EURL European Union Reference Laboratory
- EURL-FA European Union Reference Laboratory for Feed Additives
- HPLC-ICPMS High performance chromatography coupled to inductively coupled plasma mass spectrometry
- ICPMS Inductively coupled plasma mass spectrometry
- FEEDAP Panel on Additives and Products or Substances used in Animal Feed

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