Safety of selenium-enriched biomass of yarrowia lipolytica as a novel food pursuant to regulation (eu) 2015/2283

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Safety of selenium-enriched biomass of *Yarrowia lipolytica* as a novel food pursuant to Regulation (EU) 2015/2283

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Abstract

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver an opinion on selenium-enriched biomass of *Yarrowia lipolytica* as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF is the dried and heat-killed selenium-enriched biomass of *Y. lipolytica*. This yeast species is widespread in nature, can be found in the environment and in foods, and was attributed the qualified presumption of safety (QPS) status for production purposes in 2018, including food and feed products based on biomass of the yeast. The production process, fermentation in the presence of sodium selenite, includes a heat-killing step of the yeast, resulting in the absence of viable *Y. lipolytica* in the NF. The maximum total selenium content in the NF is 200 μg Se/g, mainly present as organic selenium compounds. The applicant proposed to use the NF as a food supplement. The target population proposed by the applicant is the general population from 3 years of age onwards, with maximum proposed use levels of 0.2 g/day for children from 3 to 9 years of age and 1 g/day thereafter. The Panel considers that the yeast biomass is not of safety concern at the proposed use levels. The Panel also considers that the selenium provided by the NF is as safe as selenium from other dietary sources. However, the Panel notes that, at the use levels proposed by the applicant, the intake of the NF could, in combination with a background diet high in selenium, lead to total selenium intakes exceeding the UL for selenium in all target population groups, except for children from 7 to 9 years. Furthermore, the Panel considers that newly emerging data warrant a reassessment of the UL for selenium.

Keywords: selenium-enriched *Yarrowia lipolytica*, yeast, novel food, safety

Requestor: European Commission following an application by Skotan S.A. (Poland)

Question number: EFSA-Q-2018-00796

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1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

On 22 August 2018, Skotan S.A. submitted a request to the European Commission in accordance with Article 10 of Regulation (EU) No 2015/2283[1] to place selenium-enriched biomass from *Yarrowia lipolytica* on the Union market as a novel food (NF).

Selenium-enriched biomass from *Yarrowia lipolytica* is proposed for use in various foods, including food for special medical purposes, food supplements and total diet replacement foods for weight control.

The target population is the general population, from 3 years of age onwards.

On 18 February 2019, and in accordance with Article 10(3) of Regulation (EU) 2015/2283, the European Commission asked the European Food Safety Authority (EFSA) to provide a scientific opinion on selenium-enriched biomass from *Yarrowia lipolytica* as a NF.

2. Data and methodologies

2.1. Data

The safety assessment of this novel food (NF) is based on data supplied in the application and information submitted by the applicant following an EFSA request for supplementary information.

Administrative and scientific requirements for NF applications referred to in Article 10 of Regulation (EU) 2015/2283 are listed in the Commission Implementing Regulation (EU) 2017/2469.[2]

A common and structured format on the presentation of NF applications is described in the EFSA guidance on the preparation and presentation of NF applications.[3] As indicated in this guidance, it is the duty of the applicant to provide all the available (proprietary, confidential and published) scientific data, including both data in favour and not in favour to supporting the safety of the proposed NF.

This NF application does not include a request for the protection of proprietary data.

2.2. Methodologies

The assessment follows the methodology set out in the EFSA guidance on NF applications (EFSA NDA Panel, 2016) and the principles described in the relevant existing guidance documents from the EFSA Scientific Committee. The legal provisions for the assessment are laid down in Article 11 of Regulation (EU) 2015/2283 and in Article 7 of Commission Implementing Regulation (EU) 2017/2469.

This assessment concerns only risks that might be associated with consumption of the NF under the proposed conditions of use and is not an assessment of the efficacy of the NF with regard to any (claimed) benefit.

3. Assessment

3.1. Introduction

The NF which is the subject of the application is the selenium-enriched biomass of the yeast *Y. lipolytica*.

The NF falls under category (ii), i.e. food consisting of, isolated from or produced from microorganisms, fungi or algae, according to Article 3(2)(a) of Regulation (EU) No 2015/2283.

[1] Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 (2013/0435 (COD). OJ L 327, 11.12.2015, p. 1–22.

[2] Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. OJ L 351, 30.12.2017, pp. 64–71.

[3] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle H, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Siani A, Sjödin A, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, Poulsen M, Salminen S, Schlatter J, Arcella D, Gelbmann W, de Sesmaisons-Lecarré A, Verhagen H and van Loveren H, 2016. Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4594, 24 pp. https://doi.org/10.2903/j.efsa.2016.4594

The NF is produced by fermentation, using commonly used nutrient sources plus sodium selenite. The NF is proposed to be used in food supplements. The target population proposed by the applicant is the general population from 3 years of age onwards.

3.2. Identity of the NF

The NF is the selenium-enriched biomass of the yeast *Y. lipolytica*.

The taxonomic position of the species was first established by Van der Walt and von Arx (1980), with the following microbiological taxonomy. Kingdom: fungi; subkingdom: Dikaryota; division: Ascomycota; subdivision: Saccharomycotina; class: Saccharomycetes; order: Saccharomycetales; family: Dipodascaceae; genus: *Yarrowia*; species: *Yarrowia lipolytica*.

The species *Y. lipolytica* can be found in the 'IndexFungorum' database[4] (record number ID108643).

In 2018, the EFSA BIOHAZ Panel assessed the yeast, i.e. *Y. lipolytica*, that is used to produce the NF, and recommended this yeast for the qualified presumption of safety (QPS) status but only for production purposes, including food and feed products based on biomass (EFSA BIOHAZ Panel, 2018). The qualification 'only for production purposes' requires that there are no viable *Y. lipolytica* cells in the final product.

The Panel has previously favourably assessed the safety of *Y. lipolytica* yeast biomass as a novel food (EFSA NDA Panel, 2019).

3.3. Production process

According to the information provided, the NF is produced following Good Manufacturing Practice (GMP) and Hazard Analysis Critical Control Points (HACCP) principles.

Flow charts of the manufacturing process and detailed information on the culture conditions and media have been provided (confidential).

The first step of the manufacturing process consists of the preparation of the *Y. lipolytica* yeast inoculum. Proliferation of the yeast is continued in tanks of increasing capacity using culture media consisting of nutrient sources (confidential) commonly employed in fermentation processes. The culture conditions (i.e. temperature, aeration, pH, speed of mixing) are continuously monitored.

The main fermentation step is carried out for about 10 hours in the presence of sodium selenite (Na_2SeO_3), which is among the mineral substances authorised to be added to foods (including food supplements).[5]

After reaching a certain concentration of yeast dry matter, the selenium-enriched yeast is harvested, i.e. centrifuged, rinsed with water, and centrifuged again in order to remove remnant culture medium. Thereafter the yeast biomass is dried in a drum drier at a temperature of $> 160°C$ until a moisture content of less than 5% is achieved. During this step, the yeast cells are killed.

As noted in the previous safety assessment of *Y. lipolytica* biomass (EFSA NDA Panel, 2019), the Panel reiterates that in order to monitor the efficiency of the heat treatment and to guarantee that there are no viable *Y. lipolytica* cells remaining in the dried biomass, testing for the presence of viable yeast cells has to be carried out immediately after the heat treatment (see also Specifications, Table 4).

The Panel also notes that it has to be ensured that no cross-contamination occurs with viable *Y. lipolytica* in the final steps of the manufacturing process (packaging and storage).

The Panel considers that the production process is sufficiently described and does not raise safety concerns.

3.4. Compositional data

The applicant provided batch-to-batch analysis for five batches of the NF (at a production scale of $\geq$ 1000 L, with sodium selenite as the source for selenium) for total selenium content, selenium speciation, proximate analysis and microbial counts (Table 1).

[4] http://www.indexfungorum.org/names/names.asp

[5] Commission Regulation (EC) No 1170/2009 of 30 November 2009 amending Directive 2002/46/EC of the European Parliament and of Council and Regulation (EC) No 1925/2006 of the European Parliament and of the Council as regards the lists of vitamin and minerals and their forms that can be added to foods, including food supplements, OJ L 314, 1.12.2009, p. 36–42.

Table 1: Batch-to-batch analysis of the NF

Parameter (unit)	Batch number				
	S01-19	**S02-19**	**S03-19**	**S04-19**	**S05-19**
Total selenium (μg/g)	179	176	177	174	168
Se-methionine (μg/g)(1)	124	121	120	117	112
Se-cysteine (μg/g)(1)	20	18	18	18	17
Protein (%)	43.7	43.9	44.3	43.9	44.3
Dietary fibre (%)	31.7	31.5	31.7	31.0	29.9
Sugars (%)	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2
Fat (%)	11.8	11.6	11.6	11.7	11.6
Dry matter (%)	96.6	96.8	96.9	96.9	96.8
Water (%)	3.4	3.2	3.1	3.1	3.2
Ash (%)	9.5	9.7	9.8	9.7	9.7
Contaminants					
Cadmium (mg/kg)	0.026	0.028	0.027	0.026	0.027
Mercury (mg/kg)	0.015	0.016	0.016	0.016	0.016
Lead (mg/kg)	0.044	0.044	0.045	0.042	0.043
Microbials					
TAMC (CFU/g)	6.5×10^3	1.9×10^3	3.5×10^3	5.5×10^3	1.4×10^3
TYMC (CFU/g)	< 10	< 10	< 10	< 10	< 10
Number of coliforms (CFU/g)	< 10	< 10	< 10	< 10	< 10
Salmonella spp. (in 25 g)	Not detected	Not detected	Not detected	Not detected	Not detected

TAMC: total aerobic microbial count, TYMC: total yeast and mould count, CFU: colony forming units, Se: selenium.
(1): Se-methionine and Se-cysteine as selenium.

The Panel notes the consistent results of the batch-to-batch testing of the NF showing an average content of total selenium of 175 μg Se/g with a SD of 4 μg Se/g. On average, 68% of this total selenium is Se-methionine (range 67–69%), and 10% is Se-cysteine (range 10–11%).

Nutritional analyses were provided for two additional batches of the NF.

Information was submitted on the accreditation of the laboratories that conducted the analyses presented in the application.

The Panel considers that the information provided on the composition of the NF is sufficient and does not raise safety concerns.

3.4.1. Stability

In order to demonstrate the stability of the NF, the applicant submitted results of stability testing performed for 12 months at ambient conditions (20°C and 40–60% relative humidity (RH)) (Table 2). Four batches of the NF were analysed. The parameters investigated were the content of total selenium, water, protein, fat, total aerobic microbial count (TAMC), total yeast and mould count (TYMC), coliforms and *Salmonella*. *Salmonella* and Coliforms were not detected (i.e. absent in 25 g and 1 g, respectively) in any sample over the testing period. Protein and fat contents decreased slightly over time. Results for total selenium content, TAMC, TYMC and water content are shown in Table 2.

Table 2: Stability testing at ambient conditions for selenium (μg/g), TAMC (CFU/g), TYMC (CFU/g) and water content (in %)

Batch #	Param.	Time (in months)											
		1	2	3	4	5	6	7	8	9	10	11	12
SAJ45	Selenium	248	247	247	247	245	245	244	244	243	242	241	239
	TAMC	110	80	72	50	22	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	TYMC	30	18	12	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	3.7	3.9	3.6	3.3	2.9	2.8	2.6	2.7	2.5	2.3	2.1	2.2
SAK51	Selenium	231	230	230	230	229	229	228	228	227	226	226	226
	TAMC	80	75	72	60	48	33	22	10	< 10	< 10	< 10	< 10
	TYMC	20	15	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	3.0	3.1	3.4	2.9	2.7	2.4	2.1	1.8	1.3	1.4	1.2	1.1
SAK52	Selenium	254	250	253	252	251	251	249	249	248	247	245	244
	TAMC	40	32	20	15	10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	TYMC	10	12	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	2.2	2.0	2.1	2.1	2.0	1.8	1.7	1.8	1.9	1.9	1.7	1.8
SAK53	Selenium	223	224	223	221	220	219	217	216	216	214	213	212
	TAMC	130	110	100	110	75	62	50	37	24	10	< 10	< 10
	TYMC	60	52	40	32	15	10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	4.7	4.7	4.8	4.7	4.5	4.5	4.4	4.2	4.0	3.9	3.6	3.2

TAMC: total aerobic microbial count, TYMC: total yeast and mould count, CFU: colony forming units.
The numbers of the microbial counts have to be multiplied by 10 in order to account for the dilution factor.

In addition, the applicant provided stability tests with one batch (Nr. SAJ44) of the NF with testing performed at standard storage conditions (30°C and at 65% RH) and at accelerated conditions (40°C and at 75% RH) up to 6 months (Table 3). The batch of the NF was analysed for its content of selenium, water, protein, B-group vitamins (thiamine, riboflavin, biotin, folic acid, vitamins B6 and B12; not shown) and for microbial counts.

Table 3: Stability testing at standard storage conditions and at accelerated (Acc.) conditions for one batch (#SAJ44)

Parameter	0 months	3 months		6 months	
		Standard	Acc.	Standard	Acc.
Selenium (μg/g)	219.4	213.6	249.1	217.7	221.5
Water (%)	2.8	1.4	1.6	1.0	0.9
Protein (%)	42.82	43.15	43.33	45.60	43.15
TAMC (CFU/g)	< 10	–	–	< 10	< 10
TYMC (CFU/g)	< 10	–	–	< 10	< 10
S. aureus (in 1 g)	Absent	–	–	Absent	Absent
E. coli (in 1 g)	Absent	–	–	Absent	Absent
Salmonella spp. (in 10 g)	Absent	–	–	Absent	Absent
Pseudomonas aeruginosa (in 1 g)	Absent	–	–	Absent	Absent
Bile-tolerant Gram-negative bacteria (in 1 g, qualitative test)	Absent	–	–	Absent	Absent
Bile-tolerant Gram-negative bacteria (in 1 g, quantitative test)	< 10	–	–	< 10	< 10

TAMC: total aerobic microbial count; TYMC: total yeast and mould count; CFU: colony forming units.

Given the absence of relevant changes in the composition of the NF under ambient conditions for up to 12 months and accelerated storage conditions for up to 6 months, the applicant proposed a shelf-life of 12 months for the NF.

The Panel notes that the batches analysed for the stability testing contained higher selenium concentrations than set out in the specifications for the NF. However, since the selenium is not

expected to have a major influence on the stability, the Panel considers that the data provided sufficient information with respect to the stability of the NF during 12 months.

3.5. Specifications

The specifications of the NF are indicated in Table 4.

Table 4: Specifications of the NF

Parameter	Amount	Method
Total selenium	165–200 μg/g	PN-EN ISO 17294-2:2006
Se-methionine(1)	100–140 μg/g	HPLC – ICP MS
Protein	40–50 g/100 g	PN-A-79005-7:1997 orPN-EN ISO 8968-1:2014-03
Dietary fibre	24–32 g/100 g	AOAC 985.29 orPN-A-79011-15:1998
Sugars	< 1.0 g/100 g	PN-A-74252:1998
Fat	6.0–12.0 g/100 g	AOAC 922.06 orPN-ISO 1444:2000
Total ash	≤ 15%	PN-ISO 928:1999
Water	≤ 5%	PN-EN ISO 665:2004
Dry matter	≥ 95%	PN-EN ISO 665:2004
Heavy metals		
Lead	≤ 3.0 mg/kg	PN-EN ISO 17294-2:2006
Cadmium	≤ 1.0 mg/kg	PN-EN ISO 17294-2:2006
Mercury	≤ 0.1 mg/kg	PN-EN 13804:2013-06 + ASA mercury analyser or PN-EN 13806:2003
Microbiological		
TAMC	≤ 5×10^3 CFU/g	PN-EN ISO 4833:2004 + AP1:2005
TYMC	≤ 10^2 CFU/g	PN-ISO 7954:1999
Viable *Yarrowia lipolytica* cells(2)	< 10 CFU/g (i.e. limit of detection)	PN-ISO 7954:1999
Coliforms	≤ 10 CFU/g	PN-ISO 4832:2007
Salmonella spp.	Absent in 25 g	PN-EN ISO 6579:2003

TAMC: total aerobic microbial count; TYMC: total yeast and mould count; CFU: colony forming units; HPLC: high-performance liquid chromatography; ICP MS: inductively coupled plasma mass spectrometry.
(1): Expressed as selenium.
(2): To be tested immediately after the heat-treatment step. Measures have to be in place to prevent cross-contamination with viable *Yarrowia lipolytica* cells during packaging and/or storage of the NF.

The Panel considers that the information provided on the specifications of the NF is sufficient and does not raise safety concerns.

3.6. History of use of the NF and/or of its source

There is no history of consumption of the NF.

The yeast, i.e. *Y. lipolytica*, which is used to produce the NF, is widespread in nature and can naturally be found in foods high in fat and protein (e.g. cured meat, dairy products, various types of cheese).

In 2019, the EFSA NDA Panel favourably assessed the safety of *Y. lipolytica* yeast biomass as a novel food (EFSA NDA Panel, 2019).

Also in 2019, *Y. lipolytica* heat-killed yeast biomass was authorised for the placing on the market in/as food supplements, excluding food supplements for infants and young children (Commission Implementing Regulation (EU) 2019/766[6]).

[6] Commission Implementing Regulation (EU) 2019/760 of 13 May 2019 authorising the placing on the market of *Yarrowia lipolytica* yeast biomass as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commission Implementing Regulation (EU) 2017/2470 (Text with EEA relevance.) OJ L 125, 14.5.2019, p. 13–15.

3.7. Proposed uses and use levels and anticipated intake

3.7.1. Target population

The target population as proposed by the applicant is the general population from 3 years of age onwards.

3.7.2. Proposed uses and use levels

Following a request for clarification on the proposed uses, the applicant stated that the NF is proposed to be used in food supplements only (in the form of soft or hard capsules, tablets or loose powder).

The maximum doses of the NF proposed by the applicant are 0.2 g per day for children from 3 to 9 years of age and 1 g per day thereafter (i.e. for adolescents and adults).

3.8. Absorption, distribution, metabolism and excretion (ADME)

No ADME data have been provided for the NF.

3.9. Nutritional information

In its opinion on the safety of *Y. lipolytica* yeast biomass, the Panel concluded that taking into account the composition and the proposed conditions of use, the consumption of *Y. lipolytica* yeast biomass is not nutritionally disadvantageous (EFSA NDA Panel, 2019). This conclusion was based on the nutritional analysis of *Y. lipolytica* biomass (which comprised information on the protein content, amino acid composition, carbohydrates, fibre, fatty acids, vitamins and minerals) and the proposed conditions of use (i.e. up to 3 g/day for children from 3 to 9 years of age and up to 6 g/day thereafter) (EFSA NDA Panel, 2019).

For the NF subject to the current assessment, i.e. Se-enriched *Y. lipolytica*, the applicant proposed maximum intakes of 0.2 g/day for children from 3 to 9 years of age and 1 g/day for adolescents (10–17 years) and adults.

The applicant was informed that when taking into account the intake of selenium via the background diet (EFSA NDA Panel, 2014), the consumption of the NF at the proposed use levels would lead to cumulative selenium intakes exceeding the Tolerable Upper Intake Levels (UL) for selenium as set by the Scientific Committee on Food (SCF, 2000). Therefore, the applicant was requested to reconsider and revise the proposed conditions of use. In reply, the applicant lowered the maximum specified total selenium concentration in the NF from 240 μg/g to 200 μg/g.

Previously performed intake assessments (EFSA NDA Panel, 2014) indicated average dietary selenium intakes from 20.6 to 45.9 μg/day for children aged 3–9 years, from 33.9 to 60.3 μg/day for adolescents (10–17 years) and from 31.0 to 65.6 μg/day for adults. High intakes (at the 95th percentile) ranged from 31.3 to 71.5 μg/day for children aged 3–9 years, from 55.9 to 95.5 μg/day for adolescents and from 49.6 to 113.0 μg/day for adults. The Panel recommended that the results should be considered indicative and be interpreted with caution, due to uncertainties on how accurately the information contained in the nutrient composition database reflects the variability in selenium concentrations in foods (EFSA NDA Panel, 2014).

Considering a maximum selenium concentration in the NF of 200 μg Se/g, the high (i.e. P95) dietary selenium intakes (as estimated in 2014) were used for the intake scenario for the various target population groups as proposed by the applicant (Table 5).

Table 5: Intake scenario for selenium, based on P95 dietary Se-intakes and the use of the NF as proposed by the applicant considering a maximum selenium concentration of 200 μg Se/g in the NF

Population	Age (years)	Proposed use of the NF	Se from the NF (μg/d)	High (P95) dietary Se-intake (μg/d)	Combined Se-intake (μg/d)	UL(1) for Se (μg/d)
Children	3	0.2 g/d	40	71.5	111.5	**60**
	4–6					**90**
	7–9					**130**
Adolescents	10	1 g/d	200	95.5	295.5	**130**
	11–14					**200**
	15–17					**250**
Adults	≥ 18			113.0	313.0	**300**

NF: novel food.
(1): Tolerable Upper Intake Level (SCF, 2000).

The Panel notes that for all population groups, except for children from 7-9 years, the intake levels of the NF as proposed by the applicant would, in combination with a background diet high in selenium, lead to total selenium intakes which exceed the UL set for selenium (SCF, 2000).

The Panel also notes that in some countries in the EU high dietary selenium intakes in 3 years old children are already exceeding the UL for selenium (i.e. 60 μg/d) set for this age group.

In the diet selenium is mainly present in organic compounds, as L-selenomethionine and L-selenocysteine, with lower amounts in inorganic compounds, as selenate and selenite (EFSA NDA Panel, 2014). The Panel considers that the selenium compounds provided by the NF are the same as those present in other dietary sources.

3.10. Toxicological information

The applicant provided one acute oral toxicity study (Institute of Industrial Organic Chemistry/ Branch Pszczyna, 2014) in rats, according to OECD TG 420. In the study, five female Wistar rats were given (by gavage) one dose each of 2000 mg/kg body weight (bw) of the NF (corresponding to 330 μg Se/kg bw). No deaths occurred during the 14-day observation period following administration of the NF. No adverse reactions or changes in movement, behaviour and response to stimuli, skin and fur condition, eye and eyelid status, and respiratory, digestive, urinary and reproductive systems were observed. No pathological changes were seen in the animals during the macroscopic examination of tissues at the end of the study.

The applicant did not submit any further relevant toxicological studies performed with the NF.

No human studies with the NF were provided.

The Panel considers that given the QPS status for production purposes of *Y. lipolytica* (see Section 3.2), the compositional data of the NF and the fact that the production process of the NF does not raise safety concerns, no toxicological studies are needed for the safety assessment of the NF.

The UL for selenium of 300 μg/day for adults, as adopted by the SCF in 2000 was based on a no observed adverse effect level (NOAEL) of 850 μg/day for clinical selenosis in subjects exposed on a lifetime basis to selenium in their diet and drinking water. An uncertainty factor of 3 was applied, supported by three studies reporting no adverse effects for selenium intake between about 200 and 500 μg/day. On the basis of reference body weights, the UL from the adults was extrapolated to children (SCF, 2000).

The Panel notes that, in recent years, a large amount of new data relevant for the assessment of the safety of selenium intake, including large population-based randomised controlled trials (RCTs), has become available. The results of these trials may challenge the UL for selenium as established in 2000, suggesting that the safe range intake could be narrower, in line with the indication of possible adverse effects of high selenoprotein levels (Stranges et al., 2007; Lippman et al., 2009; Steinbrenner, 2013; Hatfield et al., 2014; Winther et al., 2015; Mita et al., 2017; Brigelius-Flohé and Arnér, 2018; Kikuchi et al., 2018; Peters et al., 2018; Rayman et al., 2018; Vinceti et al., 2018a,b; Kim et al., 2019). The Panel considers that newly emerging data warrant a reassessment of the UL for selenium.

3.11. Allergenicity

In its previous opinion on *Y. lipolytica* biomass, the Panel considered that the risk of allergic reactions to the biomass of *Y. lipolytica* is low (EFSA NDA Panel, 2019).

The Panel considers that the conclusion from the previous opinion also applies to the NF under assessment, i.e. selenium-enriched *Y. lipolytica* biomass.

4. Discussion

The NF is the selenium-enriched biomass of the yeast *Y. lipolytica*, which is produced by fermentation in the presence of sodium selenite.

The NF is proposed by the applicant to be used in food supplements for the general population from 3 years of age onwards. The maximum doses of the NF proposed by the applicant are 0.2 g per day for children from 3 to 9 years of age and 1 g per day thereafter (i.e. adolescents and adults), with a maximum total selenium concentration in the NF of 200 μg Se/g.

Y. lipolytica has been attributed QPS status for production purposes, including food and feed products based on biomass of the yeast. The qualification 'for production purposes' requires that there are no viable *Y. lipolytica* cells in the final product.

In 2019, the Panel has already favourably assessed the safety of *Y. lipolytica* biomass at levels up to 3 g/day for children from 3 to 9 years of age and up to 6 g/day thereafter.

Apart from one acute oral toxicity study, no relevant toxicological information was provided for the NF. The Panel considers that given the QPS status of the yeast, the compositional data of the NF and the fact that the production process of the NF does not raise safety concerns, no toxicological studies are needed for the safety assessment of the NF.

In the diet, selenium is mainly present in organic compounds, as L-selenomethionine and L-selenocysteine, with lower amounts in inorganic compounds. The Panel considers that the selenium compounds provided by the NF are the same as those present in other dietary sources and that they are, therefore, as safe as those.

The Panel considers that newly emerging data warrant a reassessment of the UL for selenium.

5. Conclusions

The Panel considers that the yeast biomass (i.e. *Y. lipolytica*) is not of safety concern at the proposed use levels.

The Panel also considers that the selenium provided by the NF is as safe as selenium from other dietary sources.

However, the Panel notes that, at the use levels proposed by the applicant, the intake of the NF could, in combination with a background diet high in selenium, lead to total selenium intakes exceeding the UL for selenium in all target population groups, except for children from 7 to 9 years.

Furthermore, the Panel considers that newly emerging data warrant a reassessment of the UL for selenium.

Steps taken by EFSA

1) Letter from the European Commission to the European Food Safety Authority with the request for a scientific opinion on the safety of selenium-enriched biomass from *Yarrowia lipolytica* as a novel food. Ref. Nr. Ares(2019)999294, dated 18 February 2019.
2) On 18 February 2019, a valid application on selenium-enriched biomass from *Yarrowia lipolytica*, which was submitted by Skotan S.A., was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2018/0605) and the scientific evaluation procedure was initiated.
3) On 3 May 2019, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
4) On 30 August 2019, additional information was provided by the applicant and the scientific evaluation was restarted.
5) During its meeting on 18 December 2019, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of selenium-enriched biomass from *Yarrowia lipolytica* as a NF pursuant to Regulation (EU) 2015/2283.

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Abbreviations

Acc	accelerated
ADME	absorption, distribution, metabolism and excretion
bw	body weight
CFU	colony forming units
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis Critical Control Points
HPLC	high-performance liquid chromatography
ICP MS	inductively coupled plasma mass spectrometry
NF	novel food
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
QPS	qualified presumption of safety
RCT	randomised controlled trial
RH	relative humidity
SD	standard deviation
Se	selenium
TAMC	total aerobic microbial count
TYMC	total yeast and mould count
UL	Tolerable Upper Intake Level