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Safety of chromium-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 chromium-enriched biomass of *Yarrowia lipolytica* as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF is the dried and heat-killed chromium-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 chromium chloride, includes a heat-killing step of the yeast, resulting in the absence of viable *Y. lipolytica* in the NF. The maximum total chromium content of the NF is 23 μg Cr/g, with the chromium present as Cr(III). 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 2 g/day for children from 3 to 9 years of age and 4 g/day thereafter. At the proposed use levels of the NF, the combined intake of chromium provided by the NF, in addition to a background diet high in chromium, would result in total chromium intakes well below the tolerable daily intake (TDI) for chromium(III) for all target population groups. The Panel concludes that the NF, chromium-enriched biomass of *Y. lipolytica*, is safe under the proposed conditions of use.

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

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Question number: EFSA-Q-2018-00769

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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 chromium-enriched biomass from *Yarrowia lipolytica* on the Union market as a novel food (NF).

Chromium-enriched biomass from *Y. 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 chromium-enriched biomass from *Y. lipolytica* as a NF.

2. Data and methodologies

2.1. Data

The safety assessment of this NF is based on data supplied in the application and information submitted by the applicant following two EFSA requests 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 chromium-enriched biomass of the yeast *Yarrowia 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 chromium chloride as a source for chromium. The NF is proposed to be used in food supplements. The target population is the general population from 3 years of age onwards.

3.2. Identity of the NF

The NF is the chromium-enriched biomass of the yeast *Yarrowia lipolytica*.

The taxonomic position of *Y. lipolytica* was first established by Van der Walt and von Arx (1980), with the following microbiological taxonomy. Kingdom: fungi; sub-kingdom: 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 of the yeast (EFSA BIOHAZ Panel, 2018). The qualification 'only for production purposes' requires that there are no viable *Y. lipolytica* cells in the final product.

The EFSA NDA 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 in 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 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 in the presence of chromium chloride, i.e. $CrCl_3$, 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 chromium-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 on 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* (EFSA NDA Panel, 2019), the Panel reiterates that in order to monitor the efficacy 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 information on chromium content, proximate analysis and microbial counts for five batches of the NF (Table 1), produced at the intended production scale (i.e. minimum culture medium of 1,000 L).

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

[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 (produced at production scale)

Parameter (unit)	Batch number				
	Cr01-19	**Cr02-19**	**Cr03-19**	**Cr04-19**	**Cr05-19**
Chromium (μg/g)	22.4	20.6	22.8	19.3	21.1
Protein (%)	43.6	45.1	46.1	47.4	44.7
Dietary fibre (%)	30.7	24.7	29.5	25.8	30.2
Sugars (%)	< 0.2	< 0.2	1.0	1.6	0.6
Fat (%)	9.5	9.0	9.3	8.5	10.7
Dry matter (%)	93.5	93.1	95.9	96.4	95.4
Water (%)	6.5	6.9	4.1	3.6	4.6
Ash (%)	9.0	9.1	10.0	10.4	9.8
Contaminants					
Cadmium (mg/kg)	0.022	0.023	0.028	0.033	0.031
Mercury (mg/kg)	0.012	0.029	0.024	0.027	0.027
Lead (mg/kg)	0.017	0.019	0.055	0.039	0.018
Microbials					
TAMC (CFU/g)	1.2×10^4	< 10	1.7×10^5	1.2×10^2	1.3×10^4
TYMC (CFU/g)	8×10^3	< 10	7.3×10^4	1×10^2	1.4×10^4
Coliforms (in 1 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.

In order to further analyse the nature of the chromium, the NF was subjected to a three-step sequential extraction (i.e. fractionation) and a simulated *in vitro* gastrointestinal digestion. The fractionation steps comprised water extraction and digestion by Driselase and protease, respectively. About half (50.2%) of the total content of chromium in the analysed sample was found in the water-soluble part. A further 43.9% of the chromium was polysaccharide-bound and the protein-bound fraction of chromium amounted to 4.3%. Size-exclusion high-performance liquid chromatography/inductively coupled plasma-mass spectrometry (HPLC/ICP-MS) was performed with (a) the water extract and (b) an *in vitro* gastrointestinal digestate of the NF. The chromatographic analysis confirmed the identity of chromium as trivalent, i.e. Cr(III). No peak corresponding to Cr(VI) was detected in any of the fractions.

It is noted that food is generally a reducing medium that would likely determine soluble Cr(VI) to be converted to Cr(III), whereas no oxidation of Cr(III) to Cr(VI) is expected in such a medium (EFSA CONTAM Panel, 2014), which makes the presence of Cr(VI) in the NF unlikely.

The Panel notes that for some of the batches provided (see Table 1) the microbial counts exceeded the maximum specified values. According to the information provided, those samples were taken after the packaging of the NF (i.e. at the end of the manufacturing process). In order to ascertain the microbiological quality of the NF, the applicant was requested to submit additional analyses for five batches of the NF to be sampled immediately after the heat inactivation step. The results of the additional analyses as submitted by the applicant following the EFSA request are given in Table 2.

Table 2: Additional microbiological analyses for five batches of the NF

Parameter (unit)	Batch number				
	Cr06-19	**Cr07-19**	**Cr08-19**	**Cr09-19**	**Cr10-19**
TAMC (CFU/g)	< 10	1.1×10^2	8.0×10^2	< 10	5.2×10^2
TYMC (CFU/g)	< 10	< 10	< 10	< 10	< 10
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.

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 chromium, 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 chromium content, TAMC, TYMC and water content are shown in Table 3.

Table 3: Stability testing at ambient conditions for chromium (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
CrAJ47	Chrom.	18.7	18.7	18.6	18.5	18.6	18.4	18.4	18.4	18.4	18.3	18.3	18.2
	TAMC	50	54	60	54	46	33	28	20	17	10	< 10	< 10
	TYMC	20	25	22	18	15	12	8	< 10	< 10	< 10	< 10	< 10
	Water	4.1	4.1	4.4	4.4	4.2	4.3	4.1	3.8	3.7	3.5	3.6	3.4
CrAK48	Chrom.	19.8	19.8	19.8	19.7	19.7	19.7	19.6	19.6	19.6	19.5	19.4	19.4
	TAMC	10	25	28	15	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	TYMC	10	10	< 10	< 10	< 10	< < 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	2.8	2.8	2.9	2.1	2.7	2.4	2.2	2.5	2.2	2.0	1.8	1.7
CrAK49	Chrom.	20.2	20.1	20.2	20.1	20.1	20.0	20.0	19.9	19.9	19.9	19.9	19.8
	TAMC	100	110	82	70	60	44	33	18	< 10	< 10	< 10	< 10
	TYMC	30	20	18	15	10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	4.6	4.4	4.7	4.8	4.6	4.3	4.1	3.9	4.0	3.8	3.7	3.6
CrAK50	Chrom.	17.9	17.9	17.8	17.7	17.6	17.5	17.5	17.4	17.3	17.2	17.1	17.1
	TAMC	160	120	90	85	76	60	43	20	12	< 10	< 10	< 10
	TYMC	45	40	30	15	10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
	Water	3.2	3.3	3.6	3.4	3.3	3.1	3.0	3.0	2.8	2.7	2.8	2.6

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

In addition, the applicant performed stability tests with one batch (Nr. CrAJ46) of the NF at standard (30°C and at 65% RH) and at accelerated storage conditions (40°C and at 75% RH) for 6 months. The batch of the NF was analysed for its content of chromium, water, protein, B-group vitamins and for microbial counts. No relevant changes were observed in any parameter over the testing period at standard and accelerated conditions, respectively.

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 considers that the applicant provided sufficient information with respect to the stability of the NF up to 12 months under ambient conditions.

3.5. Specifications

The specifications of the NF are indicated in Table 4.

Table 4: Specifications of the NF

Parameter	Amount	Method
Total chromium	18–23 μg/g	PN-EN ISO 17294-2:2006
Chromium (VI)(*)	< 10 μg/kg (i.e. limit of detection)	HPLC/ICP-MS
Protein	40–50 g/100 g	PN-A-79005-7:1997 or PN-EN ISO 8968-1:2014-03
Dietary fibre	24–32 g/100 g	AOAC 985.29 or PN-A-79011-15:1998
Sugars	< 2.0 g/100 g	PN-A-74252:1998
Fat	6–12 g/100 g	AOAC 922.06 or PN-ISO 1444:2000
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	$\leq 5 \times 10^3$ CFU/g	PN-EN ISO 4833:2004 + AP1:2005
TYMC	$\leq 10^2$ CFU/g	PN-ISO 7954:1999
Viable *Yarrowia lipolytica* cells(1)	< 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

HPLC/ICP-MS: high-performance liquid chromatography/inductively coupled plasma-mass spectrometry; TAMC: total aerobic microbial count; TYMC: total yeast and mould count; CFU: colony forming units.

(1): 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.

(*): Even though the presence of chromium(VI) in the NF is unlikely (see Section 3.4), the Panel considers that this parameter should be added to the specifications 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]).

3.7. Proposed uses and use levels and anticipated intake

3.7.1. Target population

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

[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.

3.7.2. 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 2 g per day for children from 3 to 9 years of age and 4 g/day thereafter (i.e. adolescents and adults).

3.7.3. Combined intake of chromium from the NF and other sources

In 2014, chronic dietary exposure to Cr(III) was estimated by the EFSA CONTAM Panel in their risk assessment of chromium in food and drinking water (EFSA CONTAM Panel, 2014). Mean chronic dietary exposure values, across the different dietary surveys and age classes, ranged from 0.6 μg/kg body weight (bw) per day (minimum lower bound)[7] to 5.9 μg/kg bw per day (maximum upper bound).[8] The high dietary exposure (i.e. 95th percentile) ranged from 1.1 μg/kg bw per day (minimum lower bound) to 7.9 μg/kg bw per day (maximum upper bound) (excluding infants and toddlers) (EFSA CONTAM Panel, 2014).

Considering a maximum chromium concentration in the NF of 23 μg Cr/g (upper level as set in the specifications), the high (i.e. P95) dietary chromium intakes (as estimated in 2014) were used for the intake scenario for the various target population groups (Table 5).

Table 5: Intake scenario for chromium, based on high (i.e. P95) dietary Cr intakes and the use of the NF as proposed by the applicant considering a maximum chromium concentration of 23 μg Cr/g in the NF

Population	Age (years)	Proposed use of the NF (g/day)	Cr from the NF (μg/day)	Cr from the NF (μg/kg bw per day)(1)	P95 dietary Cr-intake (μg/kg bw per day)(2)	Combined Cr-intake (μg/kg bw per day)	TDI(3) for Cr(III) (μg/kg bw per day)	Comb. intake in % of the TDI
Children	3–9	2	46	2.0	7.9	**9.9**	300	3.3%
Adolescents	10–17	4	92	2.1	4.8	**6.9**		2.3%
Adults	≥ 18	4	92	1.3	2.6	**3.9**		1.3%

NF: novel food; bw: body weight.

(1): Derived by dividing the amount of chromium provided by the NF with the default body weights proposed by the Scientific Committee (EFSA Scientific Committee, 2012) (children of 3–9 years: 23.1 kg; adolescents of 10–14 years: 43.4 kg; adults: 70 kg).

(2): Dietary exposure assessment performed by the EFSA CONTAM Panel (EFSA CONTAM Panel, 2014).

(3): TDI (Tolerable Daily Intake) (EFSA CONTAM Panel, 2014); see also Section 3.10.

The combined intake of chromium from the NF taking into account a background diet high in chromium results in total chromium intakes of 9.9, 6.9 and 3.9 μg Cr/kg bw per day for children from 3 to 9 years, adolescents and adults, respectively.

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 of the NF and the proposed conditions of use, the consumption of the NF is not nutritionally disadvantageous (EFSA NDA Panel, 2019). This conclusion was based on the nutritional analysis of the NF (which comprised information on the protein content, amino acid composition, carbohydrates, fibre, fatty acids, vitamins and minerals in the NF) and the proposed conditions of use (i.e. 3 g/day for children from 3 to 9 years of age and up to 6 g/day thereafter).

The *Y. lipolytica* biomass which is subject of the current safety assessment is enriched with chromium, with up to 23 μg chromium (III) per g (i.e. upper level in the specifications). The proposed

[7] Lower bound: for results reported to be below the limit of quantification (LoQ) and limit of detection (LoD), the value was imputed as zero.

[8] Upper bound: for results reported to be below the LoD, the value was imputed as LoD, and for those below the LoQ, the value was imputed as the value reported for the LoQ.

intake (i.e. up to 2 g/day for children from 3 to 9 years of age and up to 4 g/day thereafter) would result in a chromium (III) consumption of 46 μg/day for children from 3 to 9 years and 92 μg/day thereafter.

In its Scientific Opinion on dietary reference values (DRVs) for chromium, the NDA Panel concluded that the essential function of chromium (as Cr(III)) in metabolism has not been substantiated and no average requirement (AR) and population reference intake (PRI) for chromium can be defined. The Panel also concluded that there was no evidence of beneficial effects associated with chromium intake in healthy subjects and, therefore, the setting of an adequate intake (AI) for chromium was also not appropriate (EFSA NDA Panel, 2014).

The Panel considers that taking into account the composition of the NF and the proposed conditions of use the consumption of the NF is not nutritionally disadvantageous.

3.10. Toxicological information

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

No human studies with the NF, which assessed safety-related parameters, 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.

In 2014, the EFSA Panel on Contaminants in the Food Chain (EFSA CONTAM Panel) derived a tolerable daily intake (TDI) of 300 μg Cr(III)/kg bw per day based on the NOAEL of a 2-year oral toxicity study in rats (where no adverse effects were observed even at the highest dose tested) and by applying an uncertainty factor of 1,000 (EFSA CONTAM Panel, 2014). This uncertainty factor of 1,000 contained an extra factor of 10 in order to account for the absence of adequate data on reproductive and developmental toxicity.

The Panel notes that at the proposed use levels of the NF, the combined intake of chromium provided by the NF in addition to a background diet high in chromium would result in total chromium intakes well below the TDI for all target population groups (i.e. 3.3%, 2.3% and 1.3% of the TDI for children from 3 to 9 years, adolescents and adults, respectively).

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 previous conclusion on the allergenicity of *Y. lipolytica* biomass also applies to the NF under assessment, i.e. chromium-enriched *Y. lipolytica* biomass.

4. Discussion

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

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 use levels of the NF proposed by the applicant are 2 g/day for children from 3 to 9 years of age and 4 g per day thereafter (i.e. adolescents and adults), with a maximum chromium concentration in the NF of 23 μg Cr/g and with the chromium present as Cr(III).

The Panel notes that the essentiality of chromium (as Cr(III)) in humans has not been substantiated and that the setting of a DRV for chromium was not appropriate (EFSA NDA Panel, 2014).

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 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.

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.

The Panel notes that at the proposed use levels of the NF, the combined intake of chromium provided by the NF in addition to a background diet high in chromium would result in total chromium intakes well below the TDI for chromium(III) for all target population groups.

5. Conclusions

The Panel concludes that the NF, chromium-enriched biomass of *Y. lipolytica*, is safe under the proposed conditions of use. The target population is the general population above 3 years of age.

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 chromium-enriched biomass from *Y. lipolytica* as a novel food. Ref. Nr. Ares(2019)988250, dated 18 February 2019.
2) On 18 February 2019, a valid application on chromium-enriched biomass from *Y. lipolytica*, which was submitted by Skotan S.A., was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2018/0556) 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) On 18 October 2019, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
6) On 12 December 2019, additional information was provided by the applicant and the scientific evaluation was restarted.
7) During its meeting on 23 January 2020, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of chromium-enriched biomass from *Y. lipolytica* as a NF pursuant to Regulation (EU) 2015/2283.

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Abbreviations

ADME	absorption, distribution, metabolism and excretion
AI	adequate intake
AR	average requirement
BIOHAZ	EFSA Panel on Biological Hazards
bw	body weight
CFU	colony forming units
Chrom	chromium
CONTAM	EFSA Panel on Contaminants in the Food Chain
DRV	dietary reference value
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis Critical Control Points
HPLC	high-performance liquid chromatography
ICP-MS	inductively coupled plasma-mass spectrometry
LoD	limit of detection
LoQ	limit of quantification
NDA	Nutrition, Novel Foods and Food Allergens
NF	novel food
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PRI	population reference intake
QPS	qualified presumption of safety
RH	relative humidity
TAMC	total aerobic microbial count
TDI	tolerable daily intake
TYMC	total yeast and mould count
UL	tolerable upper intake level