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Safety of yellow/orange tomato extract 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 yellow/orange tomato extract used as a novel food (NF) pursuant to Regulation (EU) 2283/2015. The NF which is the subject of the application is a carotenoid-rich extract from the yellow/orange tomato containing predominantly phytoene and phytofluene, as well as a lesser amount of beta-carotene, zeta-carotene and lycopene. The NF is produced from the tomato pulp using supercritical CO_2 extraction. The applicant proposes the use of the NF in cereal bars, functional drinks and as a food supplement in individuals above 15 years of age. For the use of the NF in cereal bars and functional drinks, the Panel considers, the target population is the general population. According to EFSA's latest exposure assessment for lycopene as a food additive (EFSA ANS Panel, 2017), the highest P95 intakes for children (< 10 and 10–17 years) and adults when combined to the use of lycopene as a food colour from natural occurrence would exceed the established acceptable daily intake (ADI) for lycopene (0.5 mg/kg body weight (bw) day). The estimated intakes of the NF would lead to an exceedance of the ADI when considering natural occurrence and exposure to lycopene when used as a food additive. Due to the absence of safety data regarding phytoene and phytofluene intake from the NF, and the contribution of the NF to the estimated high daily intakes of lycopene, the Panel considers that it cannot be established whether or not the consumption of the NF is nutritionally disadvantageous. The Panel concludes that the safety of the NF has not been established under the proposed conditions of use.

Keywords: novel foods, food supplement, yellow and orange tomato extract, carotenoids, phytoene, phytofluene, lycopene

Requestor: European Commission

Question number: EFSA-Q-2021-00201

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1. Introduction

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

On 2 March 2021, the company Lycored Ltd submitted an application to the European Commission in accordance with Article 10 of Regulation (EU) 2015/2283 to authorise the placing on the Union market of yellow/orange tomato extract as a novel food.

The applicant requests to authorise the use of yellow/orange tomato extract as a novel food in several foods, including food supplements as defined in Directive 2002/46/EC.

In accordance with Article 29(l)(a) of Regulation (EC) No 178/2002, the European Commission asks EFSA to provide a scientific opinion on yellow/orange tomato extract as a novel food in accordance with Article 10(3) of Regulation (EU) 2015/2283.

1.2. Additional information

Although lycopene is only one of the compounds present in the novel food (at maximum 5% per weight), previous EFSA Opinions on lycopene may deserve particular attention, considering that several of these Opinions expressed concern regarding over-consumption of lycopene. The safety of lycopene, one of the compounds of this novel food, has been assessed by EFSA several times. In their first assessment of the safety of lycopene as a food colour (E160d), the EFSA AFC Panel (2005) estimated exposure to lycopene from natural occurrence (coming mainly from tomatoes and tomato products) to be 0.5–5 mg and up to 8 mg per person and day, for average and high exposure, respectively, and occasional may be up to 20 mg per person and day. In that Opinion, the AFC Panel concluded that the data were not sufficient to establish an acceptable daily intake (ADI). Three years later however, when EFSA was asked to assess the safety of synthetic lycopene and lycopene from the mould *Blakeslea trispora* when used as a food colour, the AFC Panel derived an ADI of 0.5 mg/kg body weight (bw) per day for lycopene from all sources. This was done on the basis of subchronic and chronic toxicity studies in rats, a carcinogenicity and a two-generation study in rats, and developmental toxicity studies in the rat and rabbit (EFSA AFC Panel, 2008). Exposure to lycopene from its use as a food colour was estimated considering maximum permitted use levels (MPLs), and with actual use levels (based on surveys from industry), which were about 40–90% lower than the MPLs. When considering actual use levels for already authorised uses as a food colour plus exposure from proposed uses for synthetic lycopene and lycopene derived from *B. trispora*, the AFC Panel estimated that intakes of lycopene from natural sources and from its use as a food colour generally would be expected to remain within the ADI of 0.5 mg/kg bw per day, but this would not hold for the high level intakes by pre-school and school children, which could exceed the ADI by more than 200% and 100%, respectively.

In 2008, the EFSA NDA Panel assessed the safety of lycopene from tomato oleoresin, synthetic lycopene and lycopene from *B. trispora,* when used as a novel food (EFSA NDA Panel, 2008a,b,c). The NDA Panel concurred that the ADI established by the AFC Panel applies to lycopene from these sources. The Panel concluded that the exposure to lycopene for the average consumer would remain below the ADI, but that some consumers might exceed it. The Commission Decisions 2009/348/EC[1], 2009/355/EC[2] and 2009/365/EC[3] granted marketing authorisation for these novel foods but imposed to the marketing authorisation holder to perform a post-marketing monitoring program for the years 2009–2012 as a consequence of the concerns expressed in the EFSA Opinions regarding over-consumption of lycopene.

In 2010, EFSA was asked by the European Commission to perform a refined exposure assessment for lycopene as a food additive by considering lower MPLs as proposed by the industry and typical use levels and to provide intake estimates for several scenarios, including exposure to lycopene from natural occurrence (EFSA, 2010). When considering these lower MPLs for lycopene as a food additive as proposed by the industry (which later became authorised; presented as scenario 4 in Table 4 in that Opinion), the P95 estimates for the exposure to lycopene when used as a food additive in children

[1] Commission Decision of 23 April 2009 authorising the placing on the market of lycopene as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 106, 28.4.2009, p. 55–59.

[2] Commission Decision of 28 April 2009 authorising the placing on the market of lycopene oleoresin from tomatoes as novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 109, 30.4.2009, p. 47–51.

[3] Commission Decision of 28 April 2009 authorising the placing on the market of lycopene from *Blakeslea trispora* as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 111, 5.5.2009, p. 31–34.

aged 1–10 years exceeded the ADI for several EU Member States by up to 160%. When considering typical use levels of lycopene as a food additive and intakes from natural occurrence, the average exposures for children were approximately 0.2 mg/kg bw per day and around or slightly below the ADI at the 95th percentile (presented as scenario 4 in Table 6 in that Opinion). In adults, the estimated P95 exposure to lycopene from its use as a food colour and from natural occurrence was below the ADI. In that Opinion the ANS Panel concluded also that when exposure to lycopene as a novel food was also included, the exposure was much higher in all populations studied; that mean anticipated exposure in children amounted to 0.42–0.5 mg/kg bw/day and the P95 exposure was 44–55% above the ADI. Noting that the exposure estimates are already close to the ADI when considering exposure only from natural occurrence and from its use as a food additive, the ANS Panel concluded that with additional exposure to lycopene when used as a novel food, potential intakes might relatively easily exceed the ADI, particularly for children.

In 2015, EFSA was asked to provide an exposure assessment of lycopene as a novel food ingredient in the context of Regulation (EC) No 258/97, taking into account the post-marketing data collected for the years 2009–2012 and provided by the three marketing authorisation holders of lycopene (from tomato oleoresin, synthetic and from *B. trispora*). In their Opinion, the EFSA NDA Panel (2015) noted that only four non-food supplement products (three meal replacement drinks and a beverage) containing lycopene used as a novel food were identified for 2009–2012 and that none of these products remained on the market according to the Mintel's Global New Products Database query for 2013. From 31 food supplements containing lycopene as a novel food marketed between 2009 and 2012, nine of these discontinued to be marketed in 2013. In that post marketing data assessment, the Panel considered actual use levels (and not MPLs) for the use of lycopene as a food additive. When considering actual sales and product launch data, the NDA Panel concluded that intakes of naturally occurring lycopene, from its use as a food colour and as a novel food at permitted use levels do not lead to intakes above the ADI of 0.5 mg/kg bw per day for all population groups.

In their opinion on the extension of use of lycopene as a food colour to meat preparations, meat products and fruit and vegetable preparations up to 60 mg/kg, the EFSA ANS Panel performed an updated exposure estimate for lycopene using MPLs and concluded that additional exposure from the proposed extension of use would not add significantly to the intake of lycopene (EFSA ANS Panel, 2017). However, according to the updated intake estimates for lycopene at its already authorised uses as a food additive, the highest mean (among Member States) for children aged 12–35 months and children aged 3–9 years, and the highest P95 intake estimates for children aged 12–35 months, 3–9 years and 10–17 years exceeded the ADI of 0.5 mg/kg bw (Table 3 of that Opinion), without taking into account additional intakes which would come from the proposed extension of use and without considering exposure to lycopene from natural occurrence and potential intakes from its use as a novel food. For adults, the highest P95 intake estimate for lycopene coming from already authorised used at the MPL, was 0.38 mg/kg bw.

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 EFSA's requests for supplementary information.

During the assessment, the Panel identified additional data, which were not included in the application (Engelmann et al., 2011, Coyago-Cruz et al., 2019; Tanambell et al., 2020, Olmedilla-Alonso et al., 2021).

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

A common and structured format on the presentation of NF applications is described in the EFSA guidance on the preparation and presentation of a NF application (EFSA NDA Panel, 2016). 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) that are pertinent to the safety of the NF.

This NF application includes a request for protection of proprietary data in accordance with Article 26 of Regulation (EU) 2015/2283. The data requested by the applicant to be protected comprises the pharmacokinetic study, genotoxicity tests and human studies.

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.

Additional information which was not included in the application was retrieved by literature search following a search strategy and standard operating procedure as described by Dibusz and Vejvodova (2020).

This assessment concerns only the 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 regarding any claimed benefit.

3. Assessment

3.1. Introduction

The NF which is the subject of the application is an extract obtained from yellow/orange tomatoes. The NF is produced by separation of the tomato pulp, its drying and subsequent extraction using supercritical CO_2. The NF is an oil fraction of the tomato fruit and consists of mainly fat and carotenoids. The NF is proposed by the applicant to be used as a food supplement and as an ingredient in cereal bars and beverages.

The applicant indicates that, as defined by Regulation (EU) 2015/2283, Article 3, paragraph 2(iv), the NF falls under the category: 'food consisting of, isolated from or produced from plants or their parts, except when the food has a history of safe food use within the Union and is consisting of, isolated from or produced from a plant or a variety of the same species obtained by:

- traditional propagating practices which have been used for food production within the Union before 15 May 1997; or.
- non-traditional propagating practices which have not been used for food production within the Union before 15 May 1997, where those practices do not give rise to significant changes in the composition or structure of the food affecting its nutritional value, metabolism or level of undesirable substances'.

3.2. Identity of the NF

The NF is a carotenoid-rich extract from the pulp of the fruits of yellow/orange tomatoes, a hybrid cultivar of the common tomato (Lat. *Lycopersicon esculentum*) grown in outdoor open fields in Israel.

The identity of the species has been verified through the Plant List and Plants of the world online as *Lycopersicon esculentum* Mill with the following synonyms: *Solanum lycopersicum* L*; Lycopersicon lycopersicum* (L.) H. Karst and *Lycopersicon pyriforme* Dunal.

Scientific classification
Kingdom: Plantae
Order: Solanales
Family: Solanaceae
Genus: *Solanum*
Species: *Lycopersicon esculentum*

3.3. Production process

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

The yellow/orange tomatoes used for the manufacturing of the NF are grown for industrial use in outdoor open fields in Israel, with the main time for growth being from June to August and a growth period of ~ 120 days. The tomatoes are grown with the same growing practices used for tomatoes intended for market use. When the fruits are mature, they are harvested mechanically. Crude sorting is conducted in the field, where the fruits are sorted by colour (green tomatoes are discarded), and the tomatoes are transported to the processing facility.

Post-harvest, there is generally no period for storage or warehousing. The crop of tomatoes is taken to the processing facility where the extract is obtained. In the processing facility, there is a dedicated line for preparing the carotenoid extract. The first stage of the process is to obtain the dry tomato pulp, which is the physical process of preparing the carotenoid extract. In the second phase of the production process, the tomato pulp is extracted using supercritical CO_2 as extraction method. According to the applicant, this produces the tomato oleoresin, i.e. the NF, which is then packaged and undergoes quality assurance. The ratio between the weight of raw tomatoes to the weight of the produced NF is in the range from 360:1 to 1,110:1.

The Panel considers that the production process is sufficiently described.

3.4. Compositional data

The NF mainly consists of lipids including carotenoids, with lesser constituents being phytosterols.

In order to confirm that the manufacturing process is reproducible and adequate to produce on a commercial scale a product with the required characteristics, the applicant provided analytical information for five independent batches of the NF.

The physical and proximate characteristics of the yellow/orange tomato extract are described in Table 1. The extract is a viscous, dark brown liquid with a characteristic odour and a moisture content of ~ 0.1%. Ash content was analysed in five samples and was found to be < 0.1%.

The NF is an oil fraction of the dried tomato fruit pulp and therefore contains low amounts of protein and does not contain carbohydrates, sugars or dietary fibre above the limit of quantification.

Total lipid content including carotenoids, across four samples of the yellow/orange tomato extract ranges from 96.6% to 99.3%, and the protein content ranges from 0.31% to 0.46%.

Table 1: Proximates' batch to batch analysis of the NF

Parameter (unit)	Batches						Method of analysis
	#1	#2	#3	#4	#5	#6	
Moisture (%)	0.1	0.1	0.1	< 0.1	0.1	NA	Karl–Fisher titration
Ash (%)	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	NA	Gravimetry
Total lipids (g/100 g)	NA	98.04	96.59	NA	99.34	99.28	Hydrolysis-gravimetry
Protein (g/100 g)	NA	0.46	0.31	NA	0.38	0.42	In-house method based on AOAC 976.05, 950.36, 991.20 and 986.25
Sugars (g/100 g)	NA	< 2.00	< 2.00	NA	< 2.00	< 2.00	HPLC-RI
Glucose (g/100 g)	NA	< 0.40	< 0.40	NA	< 0.40	< 0.40	
Fructose (g/100 g)	NA	< 0.40	< 0.40	NA	< 0.40	< 0.40	

AOAC: Association of Official Analytical Chemists; HPLC-RI: High-performance liquid chromatography refractive index detection; NA: not analysed.

The lipid profile was determined in five representative samples of the NF and is presented in Table 2 below.

Table 2: Lipid profile batch-to-batch analysis of the NF

Parameter (unit)	Batches					Method of analysis
	#1	#2	#3	#4	#5	
Saturated fat (g/100 g)	20.5	23.5	20.7	20.8	22.8	GC-FID based on AOAC 996.06
Monounsaturated fat (g/100 g)	20.6	18.6	20.3	20.5	21.8	
Polyunsaturated fat (g/100 g) of which:	58.4	57.4	58.6	58.3	53.8	
– Omega-3 (mg/100 g)	4.7	6.9	4.9	4.8	3.6	
– Omega-6 (mg/100 g)	53.8	50.5	53.6	53.5	50.2	
Ratio omega-6/omega-3	11.5	7.4	10.9	11.1	13.9	
Trans-fatty acids in oil (g/100 g)	0.4	0.5	0.4	0.4	1.6	

GC: gas chromatography; AOAC: Association of Official Analytical Chemists; GC-FID: gas chromatography with a flame ionisation detector.

The free fatty acid content of five samples of the NF indicated a low acid value ranging from 0.16 to 0.19 mg KOH/g (acid value based on oleic acid).

The applicant performed a carotenoid profile analysis for five samples of the NF (Table 3). Total carotenoids ranged from 10% to 27%. The predominant carotenoids in the NF were phytoene and phytofluene, which ranged from 6% to 16%, followed by zeta-carotene from 2% to 6%, lycopene from 0.1% to 5% and beta-carotene from 0.1% to 0.2%.

Table 3: Carotenoid profile batch-to-batch analysis of the NF

Parameter (unit)	Batches					Method of analysis
	#1	#2	#3	#4	#5	
Total carotenoids (g/100 g)	10.8	10.1	12.1	10.7	27.5	Calculation
Lycopene (g/100 g)	0.1	0.2	0.2	1.9	5.1	HPLC-DAD
Phytoene and Phytofluene (g/100 g)	8.6	7.4	8.9	6.4	16.3	
ζ-Carotene (g/100 g)	2.0	2.2	2.7	2.3	5.9	
β-Carotene (g/100 g)	0.14	0.25	0.23	0.10	0.18	

HPLC-DAD: high-performance liquid chromatography-diode array detector.

The α-tocopherol content in the batches used for the stability studies ranged from 1.00 to 12.57 g/100 g NF. The applicant provided data on the phytosterols present in the five batches of the NF (results not shown). The NF contains around 1% phytosterols, composed mainly of stigmasterol, β-sitosterol and campesterol. The unsaponifiable matter ranges between 10 and 30 g/100 g NF.

Regarding the presence of inherent toxins in the NF, the applicant provided analytical data on the content of glycoalkaloids and alkaloids in five representative samples of the NF, presented in Table 4.

Table 4: Batch-to-batch analysis of glycoalkaloids and alkaloids in the NF

Parameter (unit)	Batches					Method of analysis
	#1	#2	#3	#4	#5	
Tomatidin (mg/kg)	0.050	0.075	0.089	0.052	0.068	LC–MS/MS
Tomatin (mg/kg)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	
alpha-Solanin (mg/kg)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	
alpha-Chaconin (mg/kg)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	
Solanidin (mg/kg)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	

LC–MS/MS: liquid chromatography–tandem mass spectrometry.

The Panel notes that the concentrations of glycoalkaloids in the NF are lower than the average concentrations in tomatoes (EFSA CONTAM Panel, 2020) and do not raise safety concerns.

The applicant also presented analytical data of certain contaminants which are summarised in Table 5.

The results of heavy metals analysis (lead, cadmium, mercury and arsenic) for five samples of the NF fall below the limits of quantification (LODs) for each heavy metal analysed and the limits of quantification (LOQs) for lead and cadmium comply with the limits for fruiting vegetables set out in Commission Regulation (EC) No 1881/2006[4] as amended.

A multi-residue screening analysis of pesticides in four of the samples of the NF was also performed (results not shown). Each of the samples tested was found to comply with the MRL for tomatoes set out in Regulation (EC) No 396/2005[5] with the LOQ being 0.01 mg/kg. The applicant also provided results for microbiological analyses of total plate count, *Escherichia coli*, *Salmonella* spp., *Staphylococcus aureus* and yeasts/mould performed in five samples of the NF which comply with Regulation (EC) No 2073/2005[6].

Additionally, the applicant performed analyses for dioxins, dioxin-like polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs) for five samples of the NF.

Table 5: Batch-to-batch analysis of contaminants in the NF

Parameter (unit)	Batches					Method of analysis
	#1	#2	#3	#4	#5	
Heavy metals						
Mercury (Hg) (mg/kg)	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	ICP-MS (in house procedure) for batch #4 and ICP-MS (based on AOAC 2011.19 and 993.14) for the rest
Cadmium (Cd) (mg/kg)	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	
Lead (Pb) (mg/kg)	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	
Arsenic (As) (mg/kg)	< 0.010	< 0.010	< 0.010	< 0.010	< 0.010	
Dioxins and dioxin-like PCBs – calculations per wet weight (upper bound results)[(a)]						
WHO-PCDD/PCDF-TEQ[(b)] (ng/kg)	0.205	0.192	0.184	0.198	0.152	GC/HRMS
WHO-PCB-TEQ (ng/kg)	NA	0.133	0.134	0.133	0.136	
WHO-PCDD/F-PCB-TEQ (ng/kg)	NA	0.326	0.318	0.331	0.288	
Polycyclic aromatic hydrocarbons (PAHs)						
Benz(a)anthracene (μg/kg)	1.4	0.9	1.7	1.4	1.5	HPLC – FD
Benzo(a)pyrene (μg/kg)	0.7	0.7	1.0	0.8	1.4	
Benzo(b)fluoranthene (μg/kg)	1.2	1.0	1.7	1.4	2.4	
Chrysene (μg/kg)	2.4	1.8	3.2	2.7	2.7	
Microbiological analysis						
Total plate count (CFU/g)	< 10/g	< 10/g	< 10/g	< 10/g	< 10/g	ISO 4833
Yeasts/Moulds (CFU/g)	< 10/g	< 10/g	< 10/g	< 10/g	< 10/g	ISO 21527
Escherichia coli in 10 g	ND	ND	ND	ND	ND	USP <2022>
Salmonella spp. in 25 g	ND	ND	ND	ND	ND	ISO 6579
Staphylococcus aureus in 10 g	ND	ND	ND	ND	ND	USP <2022>

ICP: MS inductively coupled plasma mass spectrometry; GC/HRMS: gas chromatography/high-resolution mass spectroscopy; HPLC-FD: high-performance liquid chromatography with fluorescence detection; ND: not detected; NA: not analysed; ISO: International Organization for Standardization; USP: United States Pharmacopeia; CFU: colony forming units.

(a): Upper-bound concentrations, calculated on assumption that all values of different congeners below the limit of quantification are equal to the limit of quantification.

(b): Sum of dioxins (sum of polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs)), expressed as World Health Organization (WHO) toxic equivalent using the WHO-toxic equivalency factors (WHO-TEFs of 2005) according to Regulation (EC) No 1881/2006).

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

The Panel considers that the information provided on the composition is sufficient for characterising the NF.

[4] Consolidated text: Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (Text with EEA relevance). OG L 364, 20.12.2006, p. 5–24.

[5] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.

[6] Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs. OJ L 338, 22.12.2005, p. 1–26.

3.4.1. Stability

The applicant performed stability tests with four batches of the NF. The tests were carried out at normal storage conditions at 4°C and at room temperature (25°C) for a period up to 65 months. The batches were analysed for carotenoid (lycopene, β-carotene, gamma-carotene, zeta-carotene, phytoene and phytofluene) and α-tocopherol content and the method used was HPLC-DAD.

According to the results of the stability tests performed, lycopene noted the highest decrease among the carotenoids tested at ~ 10% during the 65 months storage under 4°C and under room temperature (RT). Tocopherol decreased by ~ 6% at 4°C and 9% at RT. Overall, the results from the study indicate a relatively stable carotenoid and α-tocopherol content in the NF over a period of 65 months when stored at 4°C. Storage at room temperature led to decreases up to 18.7% in the total carotenoids at 18 and 24 months for some samples.

The applicant also examined the changes in the peroxide value (PV) of the NF in two representative batches with results indicating a two-fold increase at 4°C and a 3-fold increase at room temperature after a 12-month storage compared to the initial peroxide value at 0 months.

Considering the low moisture in the NF, further stability tests related to microbiological safety parameters were not requested. Taking into account the relatively stable carotenoid and tocopherol content in the NF for the duration of the stability tests, the applicant proposes a shelf-life of 36 months at 4°C and 18 months at room temperature.

Additionally, the applicant performed long-term stability studies in food matrices containing the NF. These studies examined the stability of the carotenoid and tocopherol content of the NF used as an ingredient in food supplements, beverages and cereal bars. The 3-year stability study with the NF in food supplements (softgel capsules) at room temperature and under accelerated conditions (40°C), both at 75% humidity, indicated a decrease of 11% in the total carotenoid content and a stable tocopherol content in the first 18 months at RT. The studies under accelerated conditions were discontinued at 3 months because of deterioration of the capsule shells at 40°C. The applicant concluded that the shelf life of the NF in softgel capsules at room temperature is 1.5 years.

The stability of one batch of concentrated beverage containing the yellow/orange tomato extract has been studied for a period of 12 months at room temperature (25°C) and at 4°C. The study found that the total carotenoids content decreased by 10.3% and 5.3% for 12 months storage under room temperature and 4°C, respectively. Additional studies performed with a diluted beverage containing the NF indicated a 14.2% and 7.1% decrease of total carotenoid level after 6 months at room temperature and 4°C, respectively. The applicant concluded that the shelf life for beverages containing the NF is 1 year at room temperature, but storage at 4°C is recommended.

The applicant also performed stability studies on two batches of cereal bars containing the NF for a period of up to 12 months under normal storage conditions (25°C and 60% humidity). The results of the study indicate that the total carotenoid content decreased by 13.4%. Based on the available data it is recommended that the shelf life is not more than 1 year at room temperature.

The Panel considers that the data provided sufficient information with respect to the stability of the NF.

3.5. Specifications

The specifications of the NF are indicated in Table 6.

Table 6: Specifications of the NF

Description: Carotenoid-rich extract from yellow/orange tomatoes	
Source: *Lycopersicon esculentum* Mill.	
Parameter	**Specification**
Appearance	Viscous, dark brown liquid
Moisture	< 0.5%
Proteins	0.2–0.6%
Total lipids	≥ 95%
Saturated fat	18–25%
Monounsaturated fat	17–24%
Polyunsaturated fat	52–63%

Trans fatty acids	≤ 2%
Unsaponifiable matter	10–30%
Acid value	0.14–0.20 mg KOH/g
Peroxide value	≤ 15 meqO_2/kg*
Carotenoids	
Total carotenoids	10–30 g/100 g
Phytoene + Phytofluene	5–22 g/100 g
beta-Carotene	0.1–0.6 g/100 g
zeta-Carotene	2–7 g/100 g
Lycopene	0.1–5 g/100 g
Heavy metals	
Lead	≤ 1 mg/kg
Cadmium	≤ 1 mg/kg
Mercury	≤ 0.1 mg/kg
Arsenic	≤ 1 mg/kg
Microbiological	
Total plate count	≤ 1,000 CFU/g
Escherichia coli	Not detected in 10 g
Salmonella spp.	Not detected in 25 g
Staphylococcus aureus	Not detected in 10 g
Yeasts/Mould	≤ 100 CFU/g

CFU: colony forming units.
*: Based on Codex Alimentarius guidelines for PV in concentrated oil (https://www.fao.org/3/y2774e/y2774e04.htm)

The Panel considers that the information provided on the specifications of the NF is sufficient.

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

There is no history of use of the NF.

The source of the NF is yellow/orange tomato (*S. lycopersicum L.*, syn. *L. esculentum* Mill.), an annual or perennial plant from the Solanaceae family. Being a common crop since the 18th century, the specific tomato type used in the production of the NF, i.e. the 'yellow/orange tomato', has been consumed in Europe, and has been cultivated using traditional breeding techniques.

3.7. Proposed uses and use levels and anticipated intake

3.7.1. Target population

The target population proposed by the applicant is individuals above 15 years of age. However, since the NF is intended by the applicant to be used also as an ingredient for the food categories 'cereal bars' and 'functional drinks', the safety assessment must consider that children also younger than 15 years of age could consume the NF when added to such foods, which cannot be excluded to be consumed by groups of the population other than the intended target population group in accordance to Commission Implementing Regulation (EU) 2017/2469, article 5(6).

3.7.2. Proposed uses and use levels

The applicant intends to market the NF for use in food supplements, at a maximum dose of 100 mg per day for individuals above 15 years of age.

The NF is also proposed by the applicant to be used as an ingredient in cereal bars and functional beverages. These food products defined using the FoodEx2 hierarchy, and the intended maximum use levels are reported in Table 7.

Table 7: Food categories and maximum use levels intended by the applicant

FoodEx2 level	FoodEx2 code	Food category	Maximum use level (mg NF/100 g)
3	A00EY	Cereal bars	286
3	A03FZ	Functional drinks[(a)]	40

(a): This food category includes: energy drinks, isotonic and sport drinks and fermented functional drinks (i.e. 'fermented non-alcoholic drinks' (with exclusion of dairy fermented drinks))'. The use of this code does not indicate a health claim under Regulation 1924/2006.

3.7.3. Anticipated intake of the NF

EFSA performed an intake assessment of the anticipated daily intake of the NF based on the applicant's proposed uses and maximum proposed use levels (Table 8) using the EFSA Dietary Exposure (DietEx) Tool[7], which is based on individual data from the EFSA Comprehensive European Food Consumption Database (EFSA, 2011).

The lowest and highest mean and 95th percentiles anticipated daily intake of the NF (on a mg/kg body weight (bw) basis), among the EU dietary surveys, are presented in Table 8.

The estimated daily intake of the NF for each population group from each EU dietary survey is available in the excel file annexed to this scientific opinion (under supporting information).

Table 8: Intake estimate of the NF resulting from its use as an ingredient for the intended food categories at the maximum proposed use levels

Population group	Age (years)	Mean intake (mg/kg bw per day)		P95 intake (mg/kg bw per day)	
		Lowest[(a)]	Highest[(a)]	Lowest[(b)]	Highest[(b)]
Infants	< 1	0.03	0.03	0.00	0.00
Young children[(c)]	1 to < 3	0.00	0.13	0.00	0.00
Other children	3 to < 10	0.00	0.17	0.00	1.25
Adolescents	10 to < 18	0.03	0.16	0.00	1.39
Adults[(d)]	≥ 18	0.03	0.25	0.00	1.72

bw: body weight.
(a): Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 20/12/2022. The lowest and the highest averages observed among all EU surveys are reported in these columns.
(b): Intakes are assessed for all EU dietary surveys available in the food comprehensive database on 20/12/2022. The lowest and the highest P95th observed among all EU surveys are reported in these columns (P95th based on less than 60 individuals are not considered).
(c): Referred as 'toddlers' in the EFSA food consumption comprehensive database (EFSA, 2011).
(d): Includes elderly, very elderly, pregnant and lactating women.

The assessment of the intake of lycopene and other carotenoids from the NF, is provided in Section 3.9 Nutritional information.

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

The applicant provided a pharmacokinetic clinical study (Unpublished report, 2019) performed in 24 healthy volunteers that consumed the NF in capsule form once a day for 28 days. The amount of NF was not given, but each capsule contained 7.33 mg phytoene, 2.06 mg phytofluene, 2.27 mg zeta-carotene, 0.18 mg β-carotene, 0.03 mg γ-carotene, 0.09 mg lycopene and 1.14 mg tocopherols. Plasma levels of phytoene, phytofluene and zeta-carotene were analysed during the 4-week study period. There was a significant inter-subject variability in baseline levels of the NF ingredients and their levels throughout the duration of the study. Plasma levels of phytoene and zeta-carotene were significantly higher from the first week, and for phytofluene from the second week, as compared to the baseline levels. Plateau concentration was achieved for phytoene in the second week, but not for phytofluene and zeta-carotene. The Panel notes that the human study suggests that phytoene, phytofluene and zeta-carotene in the NF are absorbed.

[7] https://www.efsa.europa.eu/it/science/tools-and-resources/dietex

The applicant also referred to a human study by Moran et al. (2016), which investigated the absorption and distribution kinetics of phytoene relative to lycopene in two males and two females following a phytoene diet providing 1–5 mg/day for 6 weeks and a single dose of 3.2 mg ^{13}C-phytoene on day 14 of the study. The authors observed that the labelled phytoene could already be quantified in plasma 1 h after the ingestion of the ^{13}C- phytoene dose, while plasma levels peaked at 3 and then at 24 h with a similar magnitude. The plasma half-life of phytoene was calculated to be 2.3 days, whereas that of lycopene was ~ 2.7-fold higher.

The Panel notes that there is limited ADME data on the main NF carotenoids phytoene and phytofluene in humans.

3.9. Nutritional information

The applicant provided a nutritional analysis of the NF (see Table 2, Compositional data section). The NF is mainly composed of lipids (96.6–99.3 g/100 g) of which up to 30 g are carotenoids, and contains a minor amount of proteins (0.31–0.46 g/100 g). The NF does not contain carbohydrates, sugars or dietary fibre above the limit of quantification. The full fatty acid profile of the NF shows that the main fatty acids are polyunsaturated fatty acids (54–59%).

The source of the NF are the yellow/orange tomatoes, tomato hybrid cultivars naturally high in some carotenoids. Carotenoids are widespread isoprenoid compounds synthesised by photosynthetic organisms and some of them serve as dietary precursors of vitamin A (Meléndez-Martínez et al., 2019). The carotenoid content is provided for five batches of the NF (see Table 4 in Compositional data section). From the total carotenoid content, the NF contains mostly phytoene and phytofluene (5–16 g/100 g NF), followed by zeta-carotene (2–6 g/100 g NF), lycopene (0.1–5 g/100 g) and beta-carotene (0.1–0.25 g/100 g NF).

Considering the consumption of the NF as food supplements (100 mg/day) by adults and the proposed maximum specification limits for the carotenoids present in the NF, the daily intakes for each component in mg/day are presented in table 9.

Table 9: Maximum daily intake (mg/day) of carotenoids from the NF when consumed as food supplement at 100 mg/day with maximum specifications

NF carotenoids' profile	Maximum specification limit	Maximum daily intake (mg/day)
Total carotenoids	30 g/100 g	30
Phytoene+Phytofluene	22 g/100 g	22
beta-Carotene	0.6 g/100 g	0.6
zeta-**Carotene**	7 g/100 g	7
Lycopene	5 g/100 g	5

Lycopene

The Panel notes that when considering the proposed maximum specification limit for lycopene of 5% in the NF, the P95 intakes of 1.25, 1.39 and 1.72 mg of the NF/kg bw per day estimated for other children, adolescents and adults, respectively (Table 9), would correspond to about 0.063, 0.069 and 0.086 mg lycopene/kg bw per day. Such exposure corresponds to 12.6, 13.8 and 17.2%, respectively, of the ADI for lycopene (i.e. 0.5 mg/kg bw per day). As food supplement the proposed use of 100 mg NF/day corresponds to up to 5 mg lycopene. When considering default body weights for adolescents between 14 and 18 years of age (i.e. 61.3 kg), and adults (i.e. 70 kg),[8] this corresponds to 0.08 and 0.07 mg/kg bw.

The main sources for lycopene are exposure from its use as a food additive (Table 10) and from natural occurrence.

[8] Default body weight as proposed by the EFSA Scientific Committee (2012).

Table 10: Summary of dietary exposure to lycopene (E 160d) from their use as a food additive at the current MPLs (minimum–maximum intakes across the dietary surveys in mg/kg bw per day) (source: Table 3 of ANS Panel Opinion, 2017)

	Infants (12 weeks–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (> 18 years)
Mean	0.01–0.13	0.17–0.78	0.15–0.60	0.07–0.33	0.02–0.17
95th percentile	0.03–0.43	0.46–1.29	0.34–1.21	0.18–0.66	0.06–0.38

According to the EFSA's latest exposure assessment for lycopene by the ANS Panel (2017) when it is used as a food additive, the ADI was exceeded by both the highest estimated mean and P95 intakes by children below 10 years of age. The estimated highest P95 intakes, but not the highest mean intakes, also exceeded the ADI in children between 10 and 17 years. Only in adults the ADI was not exceeded by the highest P95 exposure to lycopene when used as food colour.

Regarding intake of lycopene from natural occurrence in foods, the EFSA Opinions on the safety of lycopene (AFC Panel 2005, 2008) noted that the exposure to lycopene (coming mainly from tomatoes and tomato products) was 0.5–5 mg and up to 8 mg per person and day, for average and high exposure, respectively, and may occasionally be up to 20 mg per person per day. In 2010, the ANS Panel estimated the intake of lycopene from natural sources (ANS Panel 2010). For children, data were only available from France (3–10 years old) and UK (1.5–4.5 years old). The estimates were 0.13 and 0.14 mg/kg bw per day at the mean and 0.32 and 0.44 mg/kg bw per day at the P95 exposure, respectively. Data for adults were available only from UK. The mean estimate was 0.08 mg/kg bw per day (which corresponds to 5.6 mg for adults weighting 70 kg) and the P97.5 exposure was 0.3 mg/kg bw per day.

Other carotenoids

The yellow/orange tomato variety of the common tomato used for production of the NF has a high content of carotenoid intermediates, predominantly, the colourless phytoene and phytofluene (Coyago-Cruz et al., 2019; Tanambell et al., 2020). The concentration of these components is significantly higher than in red tomatoes reported by Engelmann et al. (2011), Biehler et al. (2012) and Meléndez-Martínez et al. (2015). According to these references, the combined content of phytoene+phytofluene in raw red tomatoes is about 1.5–1.8 mg/100 g whereas the applicant indicated that the tomatoes used for NF production contain phytoene plus phytofluene at ~ 11 mg/100 g raw yellow/orange tomatoes.

Although phytoene and phytofluene are present in widely consumed foods, such as tomatoes, carrots, citrus, apricots and other plant food sources (Meléndez-Martínez et al., 2019), data on the dietary intake of phytoene and phytofluene are sparse. The study by Biehler et al. (2012) assessed the contribution of 10 individual carotenoids from the 50 most frequently consumed food items to the total dietary carotenoid intake in Luxembourg. The study found that the national daily per capita intake for phytoene was 2.0 mg phytoene and 0.7 mg phytofluene, with phytoene and phytofluene contributing to 16% of the total dietary carotenoid intake. A more recent study retrieved by EFSA estimated the individual daily phytoene and phytofluene intakes from various commonly consumed foods in Spain at 1.89 and 0.47 mg/day, respectively (Olmedilla-Alonso et al., 2021). Considering the proposed combined maximum specification limit for phytoene+phytofluene (i.e. 22 g/100 g NF), consumption of 100 mg of the NF as a food supplement by adults would amount to 22 mg/day, which is about 10 times higher than the estimated exposure from natural occurrence. Such intake would correspond to the intake of these compounds coming from more than 1 kg red tomatoes.

The Panel notes that no Health-Based Guidance Value (HBGV) has been established for phytoene and phytofluene at the time of the adoption of this opinion.

In 2012, the ANS Panel of EFSA concluded that exposure to beta-carotene from its use as food additive and as food supplement at a level below 15 mg/day does not give rise to concerns about adverse health effects in the general population, including heavy smokers (EFSA ANS Panel, 2012). The maximum intake of beta-carotene from the NF when consumed as a food supplement at 100 mg per day would be 0.6 mg per day.

The Panel notes that there is not a tolerable upper intake level (UL) for beta-carotene set by EFSA. However, the UL for beta-carotene, as a source of vitamin A, is currently evaluated.[9]

[9] Mandate number M-2021-00058; Q number EFSA-Q-2021-00372.

The applicant also provided analytical data on alpha-tocopherol in three representative batches as a part of the stability study with the NF (results not shown). The α-tocopherol content in the NF is found to be 1.22–3.09 g/100 g NF.

Due to the absence of safety data regarding phytoene and phytofluene intake from the NF, and the contribution of the NF to the estimated high daily intakes of lycopene, the Panel considers that it cannot be established whether or not the consumption of the NF is nutritionally disadvantageous.

3.10. Toxicological information

The applicant provided two toxicological studies on the NF, which were conducted in compliance with OECD principles of good laboratory practice (GLP) (OECD, 1997) and in accordance with the test guidelines (TG) No 471 and 487 from the Organisation for Economic Co-operation and Development (OECD) (OECD, 1997, 2014).

These studies, which were claimed proprietary by the applicant, are listed in Table 11.

Table 11: List of toxicological studies with the NF

Reference	Type of study	Test system	Dose
Study No. 8447972 (Unpublished, 2020a)	Bacterial reverse mutation test (GLP, OECD TG 471)	*Salmonella* Typhimurium TA98, TA100, TA1535 and TA1537 *Escherichia coli* WP2uvrA	Up to 5,000 μg/plate (absence and presence of S9 mix)
Study No. 8447973 (Unpublished, 2021)	*In vitro* Micronucleus Test in Human Lymphocytes (GLP, OECD TG 487)	Duplicate cultures of human lymphocytes	Up to 5,000 μg/plate (absence and presence of S9 mix)

3.10.1. Genotoxicity

The applicant investigated the mutagenic potential of the NF in a bacterial reverse mutation assay using four *Salmonella* Typhimurium strains (TA1535, TA1537, TA98 and TA100) and one *Escherichia coli* strain (WP2uvrA). The test was performed in two experiments both in the presence and absence of liver microsomal fractions (S9-mix) following OECD Test 471 (Unpublished report, 2020a) with the NF in concentrations up to 5,000 μg/plate. There was no visible reduction in the growth of the bacterial background lawn at any concentration, either in the presence or absence of metabolic activation, in the first mutation test (plate incorporation method). The NF did not induce any biologically relevant increases in the frequency of revertant colonies for any of the bacterial strains, at any concentration with or without metabolic activation. It was concluded that the NF was not mutagenic in these bacterial systems.

The applicant further investigated the genotoxicity of the NF with an *in vitro* mammalian cell micronucleus test according to OECD TG 487 (Unpublished report, 2021). The clastogenic and aneugenic potential of the yellow/orange tomato extract was tested in normal human lymphocytes using a 4-h exposure in the presence and absence of a standard metabolic activation (S9) at a 2% final concentration, and a 24-h exposure in the absence of metabolic activation, followed by a 24-h incubation in presence of cytochalasin B.

The NF concentration levels used in the main experiment were selected using data from a preliminary toxicity test and ranged from 1.95 to 250 μg/mL. The maximum concentration tested was limited by the presence of precipitate in the culture medium.

The main genotoxic experiment did not indicate any statistically significant increases in the frequency of binucleate cells with micronuclei in any of the three exposure groups using a concentration range that included the lowest precipitating concentration. Based on this test the Panel concluded that under the experimental condition used, the NF was non-clastogenic and non-aneugenic to human lymphocytes *in vitro*.

The Panel notes that, in both genotoxicity studies, acetone was used as vehicle. Although potential effects of acetone were not compared to untreated controls in the micronucleus test, the percentage of micronuclei in binucleated cells for the vehicle (acetone) control corresponded to the laboratory historical negative controls, suggesting that the use of acetone as vehicle did not affect the control values.

Taking into account the test results provided and considering the nature, source and production process of the NF, the Panel considers that there are no concerns regarding genotoxicity.

3.10.2. Subchronic toxicity

The applicant did not provide a 90-day toxicity study. Instead, the applicant referred to a 90-day toxicity study for a previously adopted NF (tomato oleoresin) (EFSA NDA, 2008a). The Panel notes that the concentration for phytoene and phytofluene in tomato oleoresin assessed in 2008 was lower than in the present NF. The Panel considers that the test material is not representative of the NF and that therefore no conclusions can be drawn from this study on the safety of the NF.

3.10.3. Human data

The applicant provided two studies (Unpublished report, 2020b,c) involving 66 and 63 human subjects with a study duration of 16 and 12 weeks, respectively, and using Lumenato™ supplements as test substance for the NF.

The Panel notes that no adverse events related to the NF were reported. Because of the limitations of the study, such as the study design (one of the studies had an open-label design) and considering that no safety parameters other than reported adverse events were investigated, the Panel considers the studies provided by the applicant of limited value for the safety assessment of the NF.

3.11. Allergenicity

The NF contains 0.31–0.46% proteins from yellow/orange tomatoes.

Tomato allergy is a common and known allergy, and consumption of tomatoes and tomato products may cause allergic reactions in sensitised subjects. However, the allergenicity risk is not expected to be greater compared to that associated with normal consumption of tomatoes.

4. Discussion

The NF which is the subject of the application is a carotenoid-rich extract from the yellow/orange tomato. The extract is produced from the tomato pulp using supercritical CO_2 extraction; thus, no chemical modifications occur during the extraction process. The NF is mostly composed of lipids (> 96%) of which 10–30% are carotenoids, predominantly phytoene and phytofluene (6–16%), as well as a lesser amount of beta-carotene (0.1–0.2%), zeta-carotene (2–6%) and lycopene (0.1–5%).

The applicant intends to market the NF as a food supplement at a maximum daily intake of 100 mg/day and as a food ingredient in functional drinks and cereal bars. The target population for the use of the NF in food supplements is individuals above 15 years of age. For the use of the NF in cereal bars and functional drinks, the Panel considers that the target population is the general population. The EFSA Comprehensive European Food Consumption Database was used to estimate intakes of the NF when added to cereal bars and functional beverages.

The Panel notes that when considering the proposed maximum specification limit for lycopene of 5% in the NF, the P95 intakes of 1.25, 1.39 and 1.72 mg of the NF/kg bw per day estimated for other children, adolescents and adults, respectively, would correspond to about 0.063, 0.069, and 0.086 mg lycopene/kg bw per day. Such exposure corresponds to 12.6, 13.8 and 17.2%, respectively, of the ADI for lycopene (i.e. 0.5 mg/kg bw per day) from the NF alone. However, the main sources for lycopene are exposure from its use as a food additive and from natural occurrence. The Panel also notes that according to the latest exposure assessment for lycopene by the ANS Panel (2017) when it is used as a food additive, the ADI was exceeded by both the highest estimated mean and P95 intakes by children below 10 years of age. The estimated highest P95 intakes, but not the highest mean intakes, also exceeded the ADI in children between 10 and 17 years. In adults, the ADI was not exceeded by the highest estimated mean (i.e. 0.17 mg/kg bw per day) and P95 (i.e. 0.38 mg/kg bw per day) exposure to lycopene when used as food colour. This was also the case when estimated mean intakes of lycopene from natural occurrence (about 5 mg per day or 0.07 mg/kg bw per day) were added. However, combining the highest P95 estimates for lycopene exposure when used as a food colour plus high exposure estimates for naturally occurring lycopene, would reach or even exceed the ADI also in adults.

The estimated intakes of the NF would lead to an exceedance of the ADI when considering natural occurrence and exposure to lycopene when used as a food additive.

Due to the absence of safety data regarding phytoene and phytofluene intake from the NF, and the contribution of the NF to the estimated high daily intakes of lycopene, the Panel considers that it cannot be established whether or not the consumption of the NF is nutritionally disadvantageous.

5. Conclusions

The Panel concludes that the safety of the NF has not been established under the proposed conditions of use.

6. Steps taken by EFSA

1) On 06/09/2021 EFSA received a letter from the European Commission with the request for a scientific opinion on the safety of yellow/orange tomato extract as a novel food Ref.Ares(2021) 5473042.
2) On 06/09/2021, a valid application on Yellow/orange tomato extract, which was submitted by Lycored Ltd, was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2021/2369) and the scientific evaluation procedure was initiated.
3) On 24/01/2022, 13/05/2022, 07/09/2022, 29/09/2022, 14/12/2022 and 13/01/2023 EFSA requested the applicant to provide additional information and clarifications to accompany the application and the scientific evaluation was suspended.
4) On 24/04/2022, 18/08/2022, 22/09/2022, 24/11/2022, 15/12/2022 and 16/01/2023 additional information was provided by the applicant through the Commission e-submission portal and the scientific evaluation was restarted.
5) During its meeting on 28/03/2023 the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of yellow/orange tomato extract as a NF pursuant to Regulation (EU) 2015/2283.

References

Biehler E, Alkerwi A, Hoffmann L, Krause E, Guillaume M, Lair ML and Bohn T, 2012. Contribution of violaxanthin, neoxanthin, phytoene and phytofluene to total carotenoid intake: assessment in Luxembourg. Journal of Food Composition and Analysis, 25, 56–65. https://doi.org/10.1016/j.jfca.2011.07.005

Coyago-Cruz E, Corella M, Moriana A, Mapelli-Brahm P, Hernanz D, Stinco CM, Beltrán-Sinchiguano E and Meléndez-Martínez AJ, 2019. Study of commercial quality parameters, sugars, phenolics, carotenoids and plastids in different tomato varieties. Food Chemistry, 277, 480–489. https://doi.org/10.1016/j.foodchem.2018.10.139

Dibusz K and Vejvodova P, 2020. Systematic literature search to assist EFSA in the preparatory work for the safety assessment of novel food applications and traditional food notifications. EFSA supporting publication 2020;EN-1774, 72 pp. https://doi.org/10.2903/sp.efsa.2019.EN-1774

EFSA (European Food Safety Authority), 2010. Revised exposure assessment for lycopene as a food colour on request from the European Commission. EFSA Journal 2010;8(1):1444, 26 pp. https://doi.org/10.2903/j.efsa.2010.1444

EFSA (European Food Safety Authority), 2011. Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment. EFSA Journal 2011;9(3):2097, 34 pp. https://doi.org/10.2903/j.efsa.2011.2097

EFSA AFC Panel (EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food), 2005. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food related to an application on the use of alpha-tocopherol containing oil suspensions and cold-water dispersible forms of lycopene from *Blakeslea trispora* as a food colour. EFSA Journal 2005;3(12):275, 17 pp. https://doi.org/10.2903/j.efsa.2005.275

EFSA AFC Panel (EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food), 2008. Scientific Opinion of the Panel on food additives, flavourings, processing aids and materials in contact with food on a request from the Commission on the safety of use of lycopene as a food colour. EFSA Journal. 2008;674, 12 pp

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2012. Statement of the safety of β-carotene use in heavy smokers. EFSA Journal 2012;10(12):2953, 45 pp. https://doi.org/10.2903/j.efsa.2012.2953

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2017. Scientific Opinion on the extension of use of lycopene (E 160d) to certain meat preparations, meat products and fruit and vegetable preparations. EFSA Journal 2017;15(12):5064, 24 pp. https://doi.org/10.2903/j.efsa.2017.5064

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2020. Scientific Opinion – Risk assessment of glycoalkaloids in feed and food, in particular in potatoes and potato-derived products. EFSA Journal 2020;18(8):6222, 190 pp. https://doi.org/10.2903/j.efsa.2020.6222

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2008a. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from the European Commission on the safety of 'lycopene oleoresin from tomatoes'. EFSA Journal 2008;6(4):675, 22 pp. https://doi.org/10.2903/j.efsa.2008.675

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2008b. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from the European Commission on the safety of synthetic lycopene. EFSA Journal 2008;6(4):676, 25 pp. https://doi.org/10.2903/j.efsa.2008.676

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2008c. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from the European Commission on the safety of 'Lycopene Cold Water Dispersible Products (CWD) from Blakeslea trispora'. EFSA Journal 2008;893, 157 pp. https://doi.org/10.2903/j.efsa.2008.893

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2015. Statement on the post-marketing monitoring of the use of lycopene. EFSA Journal 2015;13(1):3955, 11 pp. https://doi.org/10.2903/j.efsa.2015.3955

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 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

EFSA Scientific Committee, 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. https://doi.org/10.2903/j.efsa.2012.2579

Engelmann NJ, Clinton SK and Erdman JW Jr, 2011. Nutritional aspects of phytoene and phytofluene, carotenoid precursors to lycopene. Advance Nutrition, 2, 51–61. https://doi.org/10.3945%2Fan.110.000075

Meléndez-Martínez AJ, Mapelli-Brahm P, Benítez-González A and Stinco CM, 2015. A comprehensive review on the colorless carotenoids phytoene and phytofluene. Archives of Biochemical and Biophysics, 572, 188–200. https://doi.org/10.1016/j.abb.2015.01.003

Meléndez-Martínez AJ, Stinco CM and Mapelli-Brahm P, 2019. Skin carotenoids in public health and nutricosmetics: the emerging roles and applications of the UV radiation-absorbing colourless carotenoids phytoene and phytofluene. Nutrients, 11, 1093. https://doi.org/10.3390/nu11051093

Moran NE, Novotny JA, Cichon MJ, Riedl KM, Rogers RB, Grainger EM, Schwartz SJ, Erdman JW Jr and Clinton SK, 2016. Absorption and distribution kinetics of the 13C-labeled tomato carotenoid phytoene in healthy adults. Journal of Nutrition, 146, 368–376. https://doi.org/10.3945/jn.115.220525

OECD (Organisation for Economic Co-operation and Development), 1997. Test No. 471: Bacterial reverse mutation test In: OECD guidelines for the testing of chemicals, Section 4: Health effects, 11 pp.

OECD (Organisation for Economic Co-operation and Development), 2014. Test No. 475: Mammalian bone marrow chromosomal aberration test In: OECD guidelines for the testing of chemicals, Section 4: Health effects, 16 pp.

Olmedilla-Alonso B, Benítez-González AM, Estévez-Santiago R, Mapelli-Brahm P, Stinco CM and Meléndez-Martínez AJ, 2021. Assessment of food sources and the intake of the colourless carotenoids phytoene and phytofluene in Spain. Nutrients, 13, 4436. https://doi.org/10.3390/nu13124436

Tanambell H, Bishop Karen S and Quek Siew Y, 2020. Tangerine tomatoes: origin, biochemistry, potential health benefits and future prospects. Critical Reviews in Food Science and Nutrition Volume, 61, 2237–2248. https://doi.org/10.1080/10408398.2020.1775172

Unpublished report, 2019. Analysis of effect of multiple oral administration of Lumenato (Golden Tomato) capsules to healthy volunteers on the plasma levels of phytoene, phytofluene, lycopene and zeta-carotene phytonutrients Department of Clinical Biochemistry and Pharmacology Faculty of Health Sciences Ben-Gurion University of the Negev Beer-Sheva, Israel. Unpublished document.

Unpublished report, 2020a. Carotenoids extract from Yellow/Orange Tomatoes: Reverse Mutation Assay 'Ames Test' using Salmonella typhimurium and Escherichia coli Covance Laboratories Limited, Derbyshire, United Kingdom. Unpublished document.

Unpublished report, 2020b. A Double-Blind, Randomized, Placebo-Controlled Study Evaluating the Nutritional Supplement Lumenato and its Impact on Skin Parameters in Healthy Female Subjects Lycored Ltd. TTC Co., Ltd., Japan. Unpublished document.

Unpublished report, 2020c. Open-Label Study to Assess the Impact of Lycored's Nutritional Supplement Lumenato on Skin Parameters in Healthy Women ObvioHealth, USA. Unpublished document.

Unpublished report, 2021. Carotenoids extract from Yellow/Orange Tomatoes: Micronucleus Test in Human Lymphocytes in vitro Covance Laboratories Limited, Derbyshire, United Kingdom. Unpublished document.

Abbreviations

AFC	EFSA Panel on food additives, flavourings, processing aids and materials in contact with food
ANS	EFSA Panel on Food Additives and Nutrient Sources added to Food
ADME	absorption, distribution, metabolism and excretion
ADI	acceptable daily intake

AOAC	Association of Official Analytical Chemists
bw	body weight
CFU	colony forming units
CONTAM	EFSA Panel on contaminants in the food chain
DietEx	EFSA Dietary Exposure Tool
GC	gas chromatography
GC/HRMS	gas chromatography/high-resolution mass spectroscopy
GC-FID	gas chromatography with a flame ionisation detector
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis Critical Control Points
HBGV	Health Based Guidance Value
HPLC-DAD	high-performance liquid chromatography with diode array detection
HPLC-FD	high-performance liquid chromatography with fluorescence detection
HPLC-RI	high-performance liquid chromatography with refractive index detection
ICP-MS	inductively coupled plasma mass spectrometry
ISO	International Organization for Standardization
LC–MS/MS	liquid chromatography–tandem mass spectrometry
LOD	limit of detection
LOQ	limit of quantification
MPL	maximum permitted levels
MRL	maximum residue levels
NA	not analysed
ND	not detected
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NF	novel food
OECD TG	Organisation for Economic Co-operation and Development Test Guideline
PCBs	polychlorinated biphenyls
PCDDs	polychlorinated dibenzo-*p*-dioxins
PCDFs	polychlorinated dibenzofurans
PAHs	polyaromatic hydrocarbons
PV	peroxide value
RT	room temperature
UL	tolerable upper intake level
USP	United States Pharmacopeia
WHO	World Health Organization
WHO/TEFs	World Health Organization/toxic equivalency factors

Annex A – Dietary exposure estimates to the Novel Food for each population group from each EU dietary survey

Information provided in this Annex can be found in the online version of this output (in the 'Supporting information' section).