Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004
T +1 202 637 5600
F +1 202 637 5910
www.hoganlovells.com

By FedEx

November 27, 2017

Office of Food Additive Safety (HFS–200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Re: GRAS Notice for Tomato Fruit Powder

Dear Sir or Madam:

On behalf our client, IBR Ltd. (IBR), we hereby submit the enclosed GRAS notice for tomato fruit powder as a source of phytoene and phytofluene in select foods (e.g., breakfast cereals, gravies and sauces, jams and jellies, processed vegetables and vegetable juices, snack foods, soft candies, soups and soup mixes) for consumers who intentionally seek the ingredient for its nutritional benefits at a maximum level of phytoene and phytofluene at 5 mg per serving of foods with an estimated aggregate intake of phytoene and phytofluene up to 10 mg/person/day. The statutory basis of the GRAS conclusion is scientific procedures.

Phytoene and phytofluene absorb only in the UV range and are devoid of visible color. As such, the tomato fruit powder is yellow to pale orange in color and IBR does not intend to use it as a color additive. The tomato fruit powder is not intended for use in infant formula, products under the jurisdiction of the U.S. Department of Agriculture (USDA) or any products that would require additional regulatory review by FDA. The GRAS notice does not contain any designated confidential business information. In accordance with the Agency's guidelines, we have enclosed Form 3667, one original copy of the GRAS notice, and one complete electronic copy of the GRAS notice on a compact disk (CD).

We are committed to cooperating with the Agency and believe an open dialog is one of the most effective ways to accomplish that objective. We appreciate the recommendations the Agency provided during our GRAS notice pre-submission meeting on May 4, 2017.

If you have any questions, please contact us.

Sincerely,

(b) (6)

Gary Jay Kushner
Counsel for IBR
gary.kushner@hoganlovells.com
202 637 5856

Cc:

Zhu Jianmei
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review
Jianmei.Zhu@fda.hhs.gov

GRAS Notice for Tomato Fruit Powder

Date: November 27, 2017

TABLE OF CONTENTS

1.0 GRAS STATEMENT AND CERTIFICATION

1.1 Claim of Exemption

On behalf of IBR Ltd. (IBR), Hogan Lovells US LLP (Hogan Lovells) is submitting this generally recognized as safe (GRAS) notice summarizing the data and information supporting IBR's conclusion that its intended use of PhytoflORAL® tomato fruit powder is GRAS for use in foods when used as a food ingredient at a maximum level of phytoene and phytofluene at 5 mg per serving of foods, with an estimated aggregated daily intake of 10 mg/person/day.

1.2 Name and Address of the Notifier

IBR LTD
4 Faran Street, Yavne Technological Park
Yavne, 8122503
Israel

Agent for the Notifier:

Gary Jay Kushner
Partner
Hogan Lovells US LLP
555, 13th St NW
Washington DC

1.3 Name of the Notified Substance

The name of the notified substance is "Tomato Fruit Powder" (trade name: PhytoflORAL®). The notified substance is an ingredient derived from the tomato fruits of the plant *Solanum lycopersicum* and rich in carotenoids molecules phytoene and phytofluene. PhytoflORAL® tomato fruit powder is produced in a process utilizing only physical means to process raw tomato fruits.

1.4 Intended Conditions of Use

IBR intends to use the tomato fruit powder as a source of phytoene and phytofluene in select foods (e.g., breakfast cereals, gravies and sauces, jams and jellies, processed vegetables and vegetable juices, snack foods, soft candies, soups and soup mixes) for consumers who intentionally seek the ingredient for its nutritional benefits at a maximum level of phytoene and phytofluene at 5 mg per serving of foods with an estimated aggregate intake of phytoene and phytofluene up to 10 mg/person/day.

Phytoene and phytofluene absorb only in the UV range and are devoid of visible color. As such, the tomato fruit powder is yellow to pale orange in color and IBR does not intend to use it as a color additive. PhytoflORAL® is not intended for use in infant formula, products under the jurisdiction of the U.S. Department of Agriculture (USDA) or any products that would require additional regulatory review by FDA.

1.5 Statutory Basis of GRAS Conclusion

Scientific procedures in accordance with 21 CFR § 170.30.

1.6 GRAS Statement

The notified substance is not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on IBR's conclusion that the notified substance is GRAS under the conditions of the intended use.

1.7 Availability of Information

A complete copy of the data and information that was used as a basis for this GRAS conclusion can be provided to the FDA upon request, and is also available for FDA's copying and reviewing during customary business hours at:

Hogan Lovells US LLP
555 Thirteenth Street, NW
Washington, DC 20001

1.8 GRAS Certification

To the best of our knowledge, the GRAS notice is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to us and pertinent to the evaluation of the safety and GRAS status of the use of the substance.

1.9 Signature

(b) (6)

Inon Perry
Co-founder and CEO
IBR LTD
iperry@ibrweb.com
+ 972-8-9465433

2.0 IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS, AND PHYSICAL OR TECHNICAL EFFECT

2.1 Identity

PhytoflORAL® tomato fruit powder is 100% dried tomato from a specially cultivated, non-genetically modified tomatoes (*Solanum lycopersicum*). The proprietary tomato is chosen for its higher concentration of the two specific carotenoids - phytoene and phytofluene. Tomatoes contain a complex mixture of bioactive components and nutrients, serving as a dietary source of nutrients such as potassium, folate, and the vitamins A, C, and E. 1/ As summarized in **Table 2** below, the tomato fruit powder mainly consists of protein and carbohydrates, with minor amounts of water (more than 7%), ash (no more than 15%), citric acid (up to 8.5%), and fat (up to 3.1%).

Additionally, the tomato fruit powder contains a mixture of carotenoids, including phytoene, phytofluene, and lycopene. Carotenoids are organic pigments that are produced by plants and algae. There are over 600 carotenoids found in nature and they are generally colorful orange, red, and yellow pigments synthesized by photosynthetic plants, bacteria, and fungi. The fruits of ripe tomatoes have deep red color owing to a carotenoid pigment that is synthesized during fruit ripening. 2/ As indicated by **Figure 1** below, phytoene and phytofluene are the common carotenoid precursors to the downstream carotenoid products found in plants. 3/

Phytoene and phytofluene are linear hydrocarbons with molecular formulas $C_{40}H_{64}$ (Mw= 544 Da) and $C_{40}H_{62}$ (Mw = 542 Da), respectively. Carotenoids have properties that may interrupt the course of assaults involved with UV radiation that eventually lead to skin damage. Phytofluene absorbs light in the UVA range and therefore may dampen the effect of UVA exposure. Phytoene absorbs light in the UVB and C range. These two colorless carotenoids are reported to have beneficial health effects by virtue of absorbing UV rays, when consumed orally. 4/

1/ Canene-Adams, Kirstie, et al. "The tomato as a functional food." *The Journal of nutrition* 135.5 (2005): 1226-1230.

2/ Zeb, Alam, and Sultan Mehmood. "Carotenoids Contents from Various Sources and Their Potential Health Applications." *Pakistan Journal of Nutrition* 3.3 (2004): 199-204.

3/ Engelmann, Nancy J., Steven K. Clinton, and John W. Erdman. "Nutritional aspects of phytoene and phytofluene, carotenoid precursors to lycopene." *Advances in Nutrition: An International Review Journal* 2.1 (2011): 51-61.

4/ Aust, Olivier, et al. "Supplementation with tomato-based products increases lycopene, phytofluene, and phytoene levels in human serum and protects against UV-light-induced erythema." *International journal for vitamin and nutrition research* 75.1 (2005): 54-60.

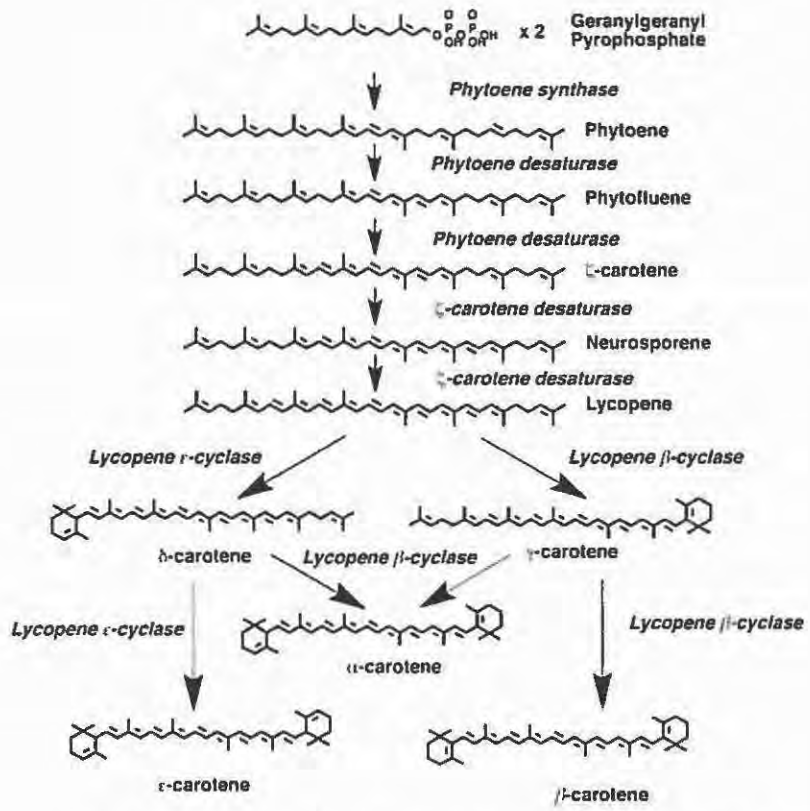

Figure 1. Carotenoid biosynthetic pathway found in plants

2.2 Characteristic Properties

PhytoflORAL® tomato fruit powder is a yellow to orange colored free flowing powder with a natural tomato taste and scent.

Table 1. Characteristic Properties of Tomato Fruit Powder	
Appearance	Free flowing powder
Color	Yellow to pale orange
Odor	Natural tomato scent
Flavor	Natural tomato taste

2.3 Quantitative Composition

PhytoflORAL® tomato fruit powder is derived from different tomato crops and subject to seasonal changes. As a result, the quantitative compositions will vary. Typical nutrient composition of the tomato fruit powder can be summarized in **Table 2**, below.

Table 2. Quantitative Composition of Tomato Fruit Powder	
Substance	**Levels (wt.%)**
Protein	15.5 – 19.5%
Fiber	10 - 65%
Moisture	< 6 %
Sugar	5 - 40%
Ash	< 15%
Citric acid	1.2 - 8.5%
Fat	0.4 - 3.1%

2.4 Manufacturing Process

PhytoflORAL® tomato fruit powder is produced in a process utilizing only physical means. The manufacturing process starts with crushing of the tomato fruits *Solanum lycopersicum*, followed by concentration, pasteurization, and freeze drying. The tomato dried powders are later milled and packaged under aseptic conditions. Powders from different crops of the fruits with certain parameters are combined to meet the specifications.

The tomato fruit powder is essentially 100% dehydrated tomato fruit with no extraneous materials. All raw materials and processing aids used in the manufacturing of tomato fruit powder meet food-grade specifications and any additional requirements or limitations outlined in applicable food regulations. Yield rate for the tomato fruit powder is 30-60:1 (i.e., 30 to 60 grams of raw tomato fruit will yield 1 g of PhytoflORAL® tomato fruit powder).

A schematic representation of the process resulting in the production of the PhytoflORAL® tomato fruit powder is presented in **Figure 2.**

Figure 2. Tomato Fruit Powder Manufacturing Process

2.5 Specifications

IRB has established the chemical and microbial specification parameters for PhytoflORAL® tomato fruit powders, which are presented in **Table 3**, below. Please note that the specifications for different grades of PhytoflORAL® may vary based on the different crops used in manufacturing.

Table 3. Chemical and Microbial Specifications of PhytoflORAL® Tomato Fruit Powder

Specification Parameter	Specification	Test Method
Phytoene and phytofluene	≥ 10 mg/g	UV-Spectrophotometry (λ286nm+λ48nm in ethanol)
Lead	< 1.0 ppm	ICP, AOAC-986.15
Arsenic	< 1.0 ppm	ICP, AOAC-986.15
Mercury	< 0.1 ppm	AA
Cadmium	< 1.0 ppm	ICP, AOAC-986.15
Copper	< 10 ppm	ICP, AOAC-986.15
Total viable counts	< 1,000 cfu/g	USP <61>/ Ph.Eur2.6.12
Yeasts and molds	< 100 cfu/g	USP <61>/ Ph.Eur2.6.12
Coliforms	Negative in 1gram	EP 2.6.13
E. coli	Negative in 1 gram	EP 2.6.13
Salmonella	Negative in 25 grams	SI885-7

Analysis of three non-consecutive lots of PhytoflORAL® tomato fruit powder has demonstrated compliance with these specifications and the results are summarized in **Table 4**, below. See **Appendix A** for certificates of analysis.

Table 4. Compliance with Specifications of Three Representative Lots

Specification Parameter	Specification	Lot No.: PK16000005-1	Lot No.: PK15480006-2	Lot No.: PK14640006-2
Phytoene and phytofluene	≥ 10 mg/g	11.34 mg/g	14.62 mg/g	14.82 mg/g
Lead	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm
Arsenic	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm
Mercury	< 0.1 ppm	< 0.1 ppm	< 0.1 ppm	< 0.1 ppm
Cadmium	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm	< 1.0 ppm
Copper	< 10 ppm	< 10 ppm	< 10 ppm	< 10 ppm
Total viable counts	< 1,000 cfu/g	Conform	Conform	Conform
Yeasts and molds	< 100 cfu/g	Conform	Conform	Conform
Coliforms	Negative in 1 gram	Conform	Conform	Conform
E. coli	Negative in 1 gram	Conform	Conform	Conform
Salmonella	Negative in 25 grams	Conform	Conform	Conform

2.6 Stability Data

Tests have shown several different production batches of PhytoflORAL® remained stable under elevated temperature (40°C) for 3 months and at room temperature for 18 months.

Please refer to **Appendix B** (Stability Report for phytoflORAL® tomato powder) for more details.

2.7 Detailed Information on Intended Use

PhytoflORAL® tomato fruit powder will be added to foods as a source of phytoene and phytofluene in select food applications (e.g., breakfast cereals, gravies and sauces, jams and jellies processed vegetables and vegetable juices, snack foods, soft candies, soups and soup mixes). Foods to which the PhytoflORAL® tomato fruit powder is added will be labeled to disclose to consumers the presence of the ingredient and its level. It is not intended to be consumed by the general population. Rather, consumers who purchase food products with PhytoflORAL® tomato fruit powders are intentionally seeking out these products for beneficial effects associated with carotenoids and their UV absorption function. The maximum use level of the ingredient is up to 5 mg of phytoene and phytofluene /serving of food. PhytoflORAL® is not intended for use in infant formula, products under the jurisdiction of the USDA or any products that would require additional regulatory review by FDA.

Since the GRAS notice only covers a narrow range of foods, and the target consumers will intentionally seek PhytoflORAL® tomato fruit powder that contain the ingredient, it would be

reasonable to assume that most consumers would eat 2 or 3 servings a day of such foods, depending on the level of PhytoflORAL® in the food. When PhytoflORAL® is added to foods at the maximum 5 mg of phytoene and phytofluene/serving, we expect consumers will not eat more than 2 serving of such foods with an aggregate daily intake up to 10 mg of phytoene and phytofluene/day.

3.0 DIETARY EXPOSURE

The health benefits associated with phytoene and phytofluene will be a primary reason why consumers will purchase and consume the food products that contain PhytoflORAL® tomato fruit powder. 5/ In addition, we estimate that such foods will be priced at a premium as compared to conventional foods that do not contain phytoene or phytofluene. As the PhytoflORAL® tomato fruit powder will be used as specialized products for consumption by consumers who intentionally seek out the ingredient in foods rather than as conventional foods for use by the general population, intakes of PhytoflORAL® tomato fruit powder were calculated on the basis of the proposed use-levels of ingredient and the direction for use. A detailed intake assessment using U.S. food consumption datasets was not conducted because the ingredient will not be consumed by the general population.

The tomato fruit powder intakes are calculated based on the proposed use levels, following the directions for use of 2 to 3 servings per day. Estimated intakes on a per kilogram body weight basis were calculated using an average adult body weight of 60 kg. With 2 servings per day, the highest estimated intake would be 2 servings per day x 5 mg/serving = **10 mg/day or 0.17 mg/kg body weight/day**.

Alternatively, the maximum intended use level of the PhytoflORAL® tomato fruit powder in food is 2 mg/kg of phytoene and phytofluene. Using the highest 2 mg/kg use level, based on FDA's default values for food consumption that a person consumes 3,000 g (or 3 kg) of food per day, we can calculate a maximum of 6 mg of phytoene and phytofluene. Since the consumption at 90th percentile for most commonly consumed foods is approximately 2 times the mean consumption for that food, the 90th percentile intake of phytoene and phytofluene can be estimated as 12 mg/day. These calculations greatly exaggerate the expected amount of PhytoflORAL® tomato fruit powder in the diet because they assume the powder will be added to all foods, rather than only certain targeted foods. Nonetheless, this exercise establishes a very conservative value of 12 mg/day, which is in line with the above assessment for the highest estimated intake at 10 mg/day.

The presence of phytoene and phytofluene has been reported for a variety of high carotenoid-containing fruits, including watermelon, apricots, cantaloupe, pink grapefruit, pumpkin, mango, papaya, peaches, prunes, and oranges, and are especially high in the aforementioned tomatoes. 6/ As discussed in more detail in **Table 5.**, when phytoene and phytofluene content was analyzed in a variety of tomato products, the more processed and therefore more dehydrated tomato products had much greater concentrations of phytoene and phytofluene (e.g. 8.36 mg, and 3.63 mg/100 g, respectively, in tomato paste) than raw tomatoes, which had concentrations of phytoene and phytofluene of 1.86 mg and 0.8 mg/100 g, respectively.

5/ As discussed in more detail in other sections of the GRAS notice, a published human study showed that an oral supplement of PhytoflORAL® tomato fruit powder at 5 mg of phytoene and phytofluene can protect the skin from UV radiation measured by a variety of indicators.

6/ *See id.*

However, the background intake data on phytoene and phytofluene are scant. The only study we identified is a study conducted by Biehler et al (2012). 7/ The daily intakes per person in the Luxembourg region analyzed was estimated to be 2.0 mg for phytoene and 0.7 mg for phytofluene. On the other hand, the consumption data on another tomato carotenoid, lycopene, are well documented in a variety of populations. In particular, Jonker et al. (2003) reported that mean lycopene intake is between 0.5 mg/p/d and 27 mg/p/d, based on a literature survey. 8/ McLain and Bausch (2003) estimates that the mean total population intake is 10.9 mg/p/d, the mean users intake is 12.2 mg/p/d, and the 90th percentile total population intake is 32.1 g/p/d, based on the CSFII, 1998 intake study. 9/ Matulka et al.(2004) estimates that the mean users intake of lycopene is 8.2 mg/p/d, with the 90th percentile intake at 15.7 mg/p/d. 10/

We can convert the level of lycopene intake to phytoene and phytofluene intake by comparing their levels in raw tomato fruits. In particular, according to the public literature, the concentration of carotenoids in tomatoes and tomato-based food products is as follows: 11/

Table 5. Concentration of Carotenoids in Tomatoes and Tomato-based Food Products (mg/100g)

Foods	Lycopene	Phytofluene	Phytoene
Raw tomato	9.25	0.80	1.86
Tomato paste	55.43	3.63	8.36
Tomato sauce	17.96	1.27	2.95
Tomato puree	16.60	1.07	2.38
Tomato juice	10.76	0.81	2.77

As the above table indicates, the weight ratio of lycopene to phytoene is around 11~15:1 in tomato fruits and tomato-based products. By the same token, the ratio of lycopene to phytoene is around 4~7:1 tomato fruits and tomato-based products. Accordingly, the average intake of 8.2 mg/p/d of lycopene reported in Matulka et al.(2004) translates to around 0.55~0.75 mg/p/d phytofluene and 1.17~2.05 mg/p/d phytoene. Notably, this intake level is consistent with the average intake of 2.0 mg for phytoene and 0.7 mg for phytofluene reported in the Biehler et al (2012).

7/ Biehler, Eric, et al. "Contribution of violaxanthin, neoxanthin, phytoene and phytofluene to total carotenoid intake: Assessment in Luxembourg." *Journal of Food Composition and Analysis* 25.1 (2012): 56-65.

8/ Jonker, D., Kuper, C.F., Fraile, N., Estrella, A. and Otero, C.R., 2003. Ninety-day oral - 3 toxicity study of lycopene fi-om Blakeslea trispora in rats. Reg. Toxicol. & Pharmacol. 37,396-406.

9/ McLain, R.M. and Bausch, J., 2003. Summary of safety studies conducted with synthetic - 4 lycopene. Reg. Toxicol. & Pharmacol. 37,274-285.

10/ Matulka, R.A., Hood, A.M. and Griffiths, J.C., 2004. Safety evaluation of a natural tomato oleoresin extract derived from food-processing tomatoes. Reg. ToxicoE. & Pharmacol. 39,390-402

11/ Perveen, Rashida, et al. "Tomato (Solanum lycopersicum) carotenoids and lycopenes chemistry; metabolism, absorption, nutrition, and allied health claims—a comprehensive review." *Critical reviews in food science and nutrition* 55.7 (2015): 919-929.

In all, the public literatures we reviewed suggest that the background intake levels of phytoene and phytofluene from the background diets are 2.0 mg for phytoene and 0.7 mg for phytofluene, respectively. Therefore, the background intake levels of phytoene and phytofluene are insignificant when compared with the intended use level of 10 mg/day by IBR.

4.0 SELF-LIMITING LEVELS OF USE

There are no physical or chemical characteristics that will limit the levels of use. However, PhytoflORAL® tomato fruit powder is added to various food applications at very specific use levels, and there is no benefit to increase the level of PhytoflORAL® beyond the current intended use, especially considering the cost of the ingredients.

5.0 Experience Based on Common Use in Food before 1958

The assessment of the safety of PhytoflORAL® is supported by the history of use of tomato fruits and processed tomato products, which have been safely consumed by humans for centuries.

We, nonetheless, recognize the proposed use of tomato fruit powder would involve its application to foods to that did not exist prior to 1958. As such, the information in this notification demonstrates the GRAS status on the basis of scientific procedures.

6.0 GRAS NARRATIVE

6.1 Safe Consumption History of Tomatoes

The assessment of the safety of PhytoflORAL® is supported by the history of use of tomato, which has been safely consumed by humans for centuries. Tomato is an integral part of diet worldwide, and especially an important component of the Mediterranean diet. Tomatoes are widely consumed both as fresh commodity and in various processed forms including canned and sun-dried tomatoes, ketchup, pastes, juices, purees, soups, sauces, and salads widely consumed before 1958 in the U.S. 12/

According to the Food Commodity Intake Database 2005-2010, which was developed by the U.S. EPA's Office of Pesticide Programs (OPP) and based on food consumption as reported eaten in WWEIA (1999-2010 survey cycles) and CSFII (1994-96/1998) surveys, 47% of total U.S. population eat tomato and the consumption can be summarized with **Table 6** below. 13/

Table 6. U.S. Consumption of Tomatoes

	N	Mean (g)	10% (g)	50% (g)	90% (g)
Commodity eaters only	21,822	59.12	9.25	40	131.84
Total population	49,343	27.58	0	0	87.34

All constituents of PhytoflORAL® powder are naturally occurring, are already present in a normal diet, and are expected to be metabolized by common metabolic pathways. Also, as discussed above, the consumption of 1 g PhytoflORAL® tomato fruit powder (which corresponds to around 10 mg of phytoene and phytofluene) is equivalent to the consumption of 30-60 g raw tomato fruits. Since the average U.S. consumer eats 59.12 g raw tomatoes per day, 1 g of PhytoflORAL® tomato fruit powder, which corresponds to about 10 mg of phytoene and phytofluene intake, is comparable to what consumers already receive from a conventional diet.

6.2 Regulatory Reviews

Several tomato fruit products that are similar to PhytoflORAL® tomato fruit powder have already been the subjects of GRAS notices that received FDA's non-objection letters.

Specifically, in GRN 000210, FDA had no questions regarding Provexis' conclusion that its water soluble tomato concentrate is GRAS, when used as an ingredient in yogurt drinks, fruit juices, and fruit flavored drinks at levels up to 3 g per serving. Provexis described the WSTC as an aqueous concentrate of tomato paste that consists of solids concentrated from a commercially available

---

12/ *See e.g.*, Clark, Faith, Berta Friend, and Marguerite C. Burk. *Nutritive value of the per capita food supply, 1909-45*. No. 616. US Department of Agriculture, 1947; Britton, Virginia. "Food consumption of 538 farm and 299 village families in Vermont." *Food consumption of 538 farm and 299 village families in Vermont.*(1941); Christensen, Raymond Peter. *Efficient use of food resources in the United States*. Vol. 963. US Department of Agriculture, 1948.

13/ Estimate based on U.S. EPA's What We Eat in America - Food Commodity Intake Database, 2005-2010 (WWEIA-FCID 2005-10).

tomato puree. The ingredient was manufactured by adding water to tomato paste, then concentrating the water-soluble tomato compounds of interest through centrifugation and membrane filtration.

Similarly, in GRN 000156, FDA had no questions regarding the notifier's determination that tomato lycopene extracts (1.5 percent and 6 percent) and crystallized tomato lycopene extract are GRAS through scientific procedures, for use as ingredients in a number of food categories (baked goods, breakfast cereals, cheeses, condiments and relishes, confections, dairy product analogs, frozen dairy desserts, gelatins, puddings and fillings, grain products, gravies and sauces, jams and jellies, meat products, milk products, processed vegetables and vegetable juices, snack foods, soft candies, soups and soup mixes), at a maximum final concentration of lycopene in food of 10 mg/kg. GRN 000156 described the chemical composition of the tomato lycopene extract (1.5 percent or 6 percent), which contains a standardized concentration of lycopene (1.5 or 6 percent respectively), with the balance consisting of other tomato lipids including total fatty acids, phytosterols, tocopherols, and other carotenoids such as phytoene, phytofluene, and beta-carotene. The manufacturing of the ingredient involves two steps: production of tomato pulp and an ethyl acetate extraction of fat-soluble components from tomato pulp.

While the GRAS notices referenced above cover tomato products different from the PhytoflORAL® tomato fruit powder, they exhibit FDA's confidence in the safety of these tomato-based ingredients. The PhytoflORAL® tomato fruit powder is produced only with physical processes and is 100% dried tomato with no extraneous materials. It does not present any safety concerns that have not been already addressed in the existing GRAS notices that have been favorably reviewed by FDA.

In addition, mixed carotenes [E 160a (i)] and beta-carotene [E 160a (ii)] are authorized as food additives in the European Union (EU) and have been evaluated previously by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). 14/ Based on the available data, both the JECFA and EU expert panel concluded that no allowable daily intake (ADI) for mixed carotenes can be established. Also notably, in 2006, the UK's Food Standards Agency concluded the PhytoflORAL® tomato fruit powder was not subject to the novel foods application because the processing of the tomatoes to produce PhytoflORAL did not introduce changes classifying PhytoflORAL® as novel.

6.3 Safety Assessment

As discussed above, FDA has already reviewed extensive safety studies on the safety of tomato ingredients in general and the carotenoid molecule lycopene through GRN 000156 and GRN 000210. Accordingly, most of our safety discussion below focuses on data that specifically evaluate phytoene and phytofluene, or tomato ingredients with phytoene and phytofluene levels disclosed.

6.3.1 Absorption, Distribution, Metabolism, and Excretion (ADME)

The absorption of dietary phytoene and phytofluene was examined in human studies. In one study, 36 healthy volunteers were randomly allocated to three groups, who ingested either synthetic

14/ Scientific Opinion on the re-evaluation of mixed carotenes (E 160a (i)) and beta-carotene (E 160a (ii)) as a food additive, EFSA Journal 2012; 10(3):2593.

lycopene, a commercial tomato extract in soft gel capsules that contained 0.4 mg phytofluene and 0.5 mg phytoene, or a commercial tomato-based drink. 15/ The basal plasma levels of the carotenoids in the three groups range between 0.27 and 0.44 nmol/mL (phytofluene) and 0.06 and 0.07 nmol/mL (phytoene). In another human study where 9 women and 7 men were administered lycopene-rich tomato juice that also contained 5.22 mg/day of phytofluene and 5.76 mg/day of phytoene, for 4 weeks, it was found that the highest proportion of the three carotenes (ranging from 65% in phytofluene to 76% in phytoene and lycopene) was in LDLs. 16/

Carotenoids, including phytoene and phytofluene, are known to accumulate in human skin (in the range of nmol/g wet tissue), notably in the forehead, palm of the hand and dorsal skin. 17/ Khachik et.al (2002) reported detection of phytoene and phytofluene in the same tissues where lycopene accumulates, including in liver, lung, breast, prostate, colon, and skin tissue. 18/ The liver is often enriched in carotenoids, and in autopsy samples, lycopene was present at a greater concentration (0.66 nmol/g) than phytoene and phytofluene (0.31 and 0.48 nmol/g, respectively). 19/

To learn more about the bioavailability of phytoene and phytofluene, Sprague-Dawley rats were fed a diet consisting of 0.1% dried algal (*Dunaliella bardawil*) powder (the algal powder contained 2% phytoene and 0.1% phytofluene). 20/ Rats were fed the carotenoid diet for 2 weeks, after which their tissues were analyzed for phytoene content. The liver had the greatest accumulation of phytoene (0.440 ± 0.024 μmol/100 g tissue) followed by the adrenals and much lesser amounts in the other tissues measured. In another study utilizing Copenhagen rats, phytoene and phytofluene bioavailability from different tomato powders were evaluated. 21/ This study showed that different carotenoid profiles and amounts present in tomato powders result in differential liver carotenoid accumulation. Notably, for the tomato powder that had overall greater carotenoids with significantly more phytoene and phytofluene, but not enhanced lycopene, the rats fed this carotenoid-enriched powder accumulated significantly more hepatic phytoene and phytofluene but the same amount of lycopene as the standard powder-fed rats.

6.3.2 Safety Studies with Tomato Products

Tomato products that contain phytoene and phytofluene have been a normal part of the human diet with a long safe consumption history. Numerous animal and clinical studies using tomato products

---

15/ *See supra* note 4.

16/ Paetau, Inke, et al. "Chronic ingestion of lycopene-rich tomato juice or lycopene supplements significantly increases plasma concentrations of lycopene and related tomato carotenoids in humans." *The American journal of clinical nutrition* 68.6 (1998): 1187-1195.

17/ Meléndez-Martínez, Antonio J., et al. "A comprehensive review on the colorless carotenoids phytoene and phytofluene." *Archives of biochemistry and biophysics* 572 (2015): 188-200.

18/ Khachik, Frederick, et al. "Chemistry, distribution, and metabolism of tomato carotenoids and their impact on human health." *Experimental biology and medicine* 227.10 (2002): 845-851.

19/ *See id.*

20/ Werman, Moshe J., Shoshana Mokady, and Ami Ben-Amotz. "Bioavailability of the isomer mixture of phytoene and phytofluene-rich alga Dunaliella bardawil in rat plasma and tissues." *The Journal of nutritional biochemistry*13.10 (2002): 585-591.

21/ Liu, Ann G., et al. "Feeding tomato and broccoli powders enriched with bioactives improves bioactivity markers in rats." *Journal of agricultural and food chemistry* 57.16 (2009): 7304-7310.

have demonstrated that consumption of these tomato products is safe and well tolerated. For example, in Moreira EA et.al (2005), twenty-four male Wistar rats were fed a diet that contains up to 25% of tomato powder in the diet (25 g/kg bw/day). 22/ The authors did not report any adverse effects. In Stoewsand GS et.al (1996), the authors conducted an 11-week rat feeding study to determine the general safety of a nematode-resistant tomato cultivar. 23/ Comparison of growth, mean blood hemoglobin, hematocrit, red blood cell count, and total white blood cell count of rats fed a complete diet containing 40% (nematode-resistant) tomato cultivar to two other groups of rats, fed either a "New Yorker" tomato (nematode-susceptible) or a control diet, showed normal and similar results. The authors concluded that the study shows no unexpected toxicants influencing animal growth and hematology. The 40% dietary level is equivalent to 40 g/kg bw/day of tomato cultivar, which can be considered the no-observed-adverse-effect level (NOAEL).

6.3.3 Safety Studies with Phytoene and Phytofluene

6.3.3.1 Genotoxicity

Ames test with *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 demonstrated that tomato fruit products with around 0.5 to 0.75% phytoene and 0.4 to 0.65% phytofluene are non-mutagenic. 24/ The findings are consistent with other studies conducted with tomatoes or tomato products. For example, Chen et.al (2003) reported a genetically-modified tomato cultivar not to be mutagenic to *Salmonella typhimurium* strains at concentrations of 0.1 to 5.0 mg/plate. 25/

6.3.3.2 Animal Studies

Rats (N=20/sex/group) were given 0, 45, 450, or 4,500 mg/kg/day of a tomato product with tomato fruit products with around 0.5 to 0.75% phytoene and 0.4 to 0.65% phytofluene for 13 weeks. 26/ The study reported no deaths during the treatment period and there were no differences in body weight gain, food intake, or food conversion efficiency between test and control animals. Test animals had no ocular lesions, changes in hematology, urinalysis changes, changes in organ weights, or macroscopic or microscopic differences from control animals. The NOAEL derived from the 13-week study was established as 4,500 mg/kg/day. This corresponds to about 40.5 mg/kg/day or 2,430 mg/day of phytoene and phytofluene. 27/

6.3.3.3 Observations in Humans

22/ Moreira, Emilia AM, et al. "Effects of diet energy level and tomato powder consumption on antioxidant status in rats." *Clinical nutrition* 24.6 (2005): 1038-1046.

23/ Stoewsand, Gilbert S., Judy L. Anderson, and Richard W. Robinson. "Safety assessment of a nematode-resistant tomato by a simple, short-term rat feeding study." *Regulatory Toxicology and Pharmacology* 24.1 (1996): 6-8.

24/ *See supra* note 10.

25/ Chen, Zhang-Liang, et al. "Safety assessment for genetically modified sweet pepper and tomato." *Toxicology* 188.2 (2003): 297-307.

26/ *See supra* note 10.

27/ 40.5 mg/kg/day = 4,500 mg/kg/day x (0.5% + 0.4%).

Many clinical studies using tomato products have demonstrated that the consumption of phytoene and phytofluene is safe and well tolerated. For example, in Aust et al. (2005), 36 healthy adult volunteers were recruited for the evaluation of tomato-based products supplementation on protection of human skin against ultraviolet (UV) light-induced erythema. 28/ The participants were randomly assigned to three groups of the same size (n = 12) for the 12-week study. In particular, participants assigned to the test group consumed two times per day 250 mL of a solubilized tomato drink. The content of carotenoids in 250 mL of this beverage was reported as 4.1 mg lycopene, 1.6 mg phytofluene, 2.3 mg phytoene, and 0.2 mg β-carotene. As such, the daily intakes of phytoene and phytofluene for the test group are 4.6 mg and 3.2 mg, respectively, or a combined intake of 7.8 mg/day. The authors concluded that phytofluene and phytoene may have contributed to UV protection. No human adverse effects were observed. In another human clinical trial, twenty-six healthy subjects consumed 250 ml of a formulated tomato drink, which provides about 6 mg lycopene, 4 mg phytoene, and 3 mg phytofluene or a placebo drink. 29/ Supplementation with the tomato drink was well tolerated, and there was no reported untoward side effects. Other recent intervention studies are summarized in **Table 7.** below and neither of these studies reported adverse side effects.

Table 7. Summary of Recent Intervention Studies Reporting Phytoene and Phytofluene

Studies	Design	Phytofluene	Phytoene
Paetau, Inke, et al. "Carotenoids in human buccal mucosa cells after 4 wk of supplementation with tomato juice or lycopene supplements." *The American journal of clinical nutrition* 70.4 (1999): 490-494.	Fifteen healthy subjects ingested lycopene-rich tomato juice, tomato oleoresin, lycopene beadlets and a placebo for 4 wk each in a randomized crossover design while consuming self-selected diets.	5·11 mg/day	5·76 mg/day
Müller, H., et al. "Plasma concentrations of carotenoids in healthy volunteers after intervention with carotenoid-rich foods." *European journal of nutrition*38.1 (1999): 35-44.	A two week carotenoid depletion period was followed by a daily consumption of 330 mL tomato juice (40 mg lycopene), then by 330 mL carrot juice (15.7 mg α-carotene and 22.3 mg β-carotene), and then by a 10 g spinach powder preparation (11.3 mg lutein and 3.1 mg β-carotene) served with main meals for two weeks, respectively.	2.3 mg/day	7·3 mg/day

28/ *See supra* note 4.

29/ Porrini, Marisa, et al. "Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection." *British Journal of Nutrition* 93.1 (2005): 93-99.

More recently, in von Oppen-Bezalel, Liki, et al. (2015), a group of 22 healthy female volunteers were given an oral supplement of PhytoflORAL® tomato fruit powder corresponding to an equivalent of 5 mg of phytoene and phytofluene a day for 12 weeks. 30/ The results suggested that the daily intake of these carotenoids can protect the skin from UV radiation measured by a variety of indicators. The PhytoflORAL® tomato fruit powder was globally well tolerated with no relevant cutaneous side effects, although a single subject suffered from possibly product-related headaches.

6.4 Safety Conclusion

The NOAEL for of a tomato product with tomato fruit products with around 0.5 to 0.75% phytoene and 0.4 to 0.65% phytofluene in rats is 4,500 mg/kg/day. This corresponds to about 40.5 mg/kg/day or 2,430 mg/day of phytoene and phytofluene. As discussed above, the maximum phytoene and phytofluene consumption levels from the existing and intended uses with the PhytoflORAL® tomato fruit powder is 10 mg/day. Even this very conservative estimate, however, is well below the 2,430 mg/day phytoene and phytofluene NOAEL levels with over a 200 margin of safety. Human studies conducted with ingredients that contain phytoene and phytofluene at comparable levels (i.e., around 10 mg/day) also demonstrate phytoene and phytofluene are well-tolerated and no adverse effects in humans were observed.

In summary, based on the demonstrated safe consumption history of tomato fruits and tomato products, as well as the safety studies we have reviewed on the safety of phytoene and phytofluene, we conclude that the intended use of PhytoflORAL® tomato fruit powder in human diets can be considered GRAS through scientific procedures.

30/ von Oppen-Bezalel, Liki, et al. "The photoprotective effects of a food supplement tomato powder rich in phytoene and phytofluene, the colorless carotenoids, a preliminary study." *Global Dermatol.* 2 (2015): 178-182.

7.0 LIST OF SUPPORTING DATA AND INFORMATION

All of the following data and information are publicly available.

Canene-Adams, Kirstie, et al. "The tomato as a functional food." *The Journal of nutrition* 135.5 (2005): 1226-1230.

Zeb, Alam, and Sultan Mehmood. "Carotenoids Contents from Various Sources and Their Potential Health Applications." *Pakistan Journal of Nutrition* 3.3 (2004): 199-204.

Engelmann, Nancy J., Steven K. Clinton, and John W. Erdman. "Nutritional aspects of phytoene and phytofluene, carotenoid precursors to lycopene." *Advances in Nutrition: An International Review Journal* 2.1 (2011): 51-61.

Aust, Olivier, et al. "Supplementation with tomato-based products increases lycopene, phytofluene, and phytoene levels in human serum and protects against UV-light-induced erythema." *International journal for vitamin and nutrition research* 75.1 (2005): 54-60.

Biehler, Eric, et al. "Contribution of violaxanthin, neoxanthin, phytoene and phytofluene to total carotenoid intake: Assessment in Luxembourg." *Journal of Food Composition and Analysis* 25.1 (2012): 56-65.

Jonker, D., Kuper, C.F., Fraile, N., Estrella, A. and Otero, C.R., 2003. Ninety-day oral - 3 toxicity study of lycopene fi-om Blakeslea trispora in rats. Reg. Toxicol. & Pharmacol. 37,396-406.

McLain, R.M. and Bausch, J., 2003. Summary of safety studies conducted with synthetic - 4 lycopene. Reg. Toxicol. & Pharmacol. 37,274-285.

Matulka, R.A., Hood, A.M. and Griffiths, J.C., 2004. Safety evaluation of a natural tomato oleoresin extract derived from food-processing tomatoes. Reg. ToxicoE. & Pharmacol. 39,390-402

Perveen, Rashida, et al. "Tomato (Solanum lycopersicum) carotenoids and lycopenes chemistry; metabolism, absorption, nutrition, and allied health claims—a comprehensive review." *Critical reviews in food science and nutrition* 55.7 (2015): 919-929.

Clark, Faith, Berta Friend, and Marguerite C. Burk. *Nutritive value of the per capita food supply, 1909-45.* No. 616. US Department of Agriculture, 1947.

Britton, Virginia. "Food consumption of 538 farm and 299 village families in Vermont." *Food consumption of 538 farm and 299 village families in Vermont.*(1941).

Christensen, Raymond Peter. *Efficient use of food resources in the United States.* Vol. 963. US Department of Agriculture, 1948.

U.S. EPA's What We Eat in America - Food Commodity Intake Database, 2005-2010 (WWEIA-FCID 2005-10).

Scientific Opinion on the re-evaluation of mixed carotenes (E 160a (i)) and beta-carotene (E 160a (ii)) as a food additive, EFSA Journal 2012; 10(3):2593.

Paetau, Inke, et al. "Chronic ingestion of lycopene-rich tomato juice or lycopene supplements significantly increases plasma concentrations of lycopene and related tomato carotenoids in humans." *The American journal of clinical nutrition* 68.6 (1998): 1187-1195.

Meléndez-Martínez, Antonio J., et al. "A comprehensive review on the colorless carotenoids phytoene and phytofluene." *Archives of biochemistry and biophysics* 572 (2015): 188-200.

Khachik, Frederick, et al. "Chemistry, distribution, and metabolism of tomato carotenoids and their impact on human health." *Experimental biology and medicine* 227.10 (2002): 845-851.

Werman, Moshe J., Shoshana Mokady, and Ami Ben-Amotz. "Bioavailability of the isomer mixture of phytoene and phytofluene-rich alga Dunaliella bardawil in rat plasma and tissues." *The Journal of nutritional biochemistry*13.10 (2002): 585-591.

Liu, Ann G., et al. "Feeding tomato and broccoli powders enriched with bioactives improves bioactivity markers in rats." *Journal of agricultural and food chemistry* 57.16 (2009): 7304-7310.

Moreira, Emilia AM, et al. "Effects of diet energy level and tomato powder consumption on antioxidant status in rats." *Clinical nutrition* 24.6 (2005): 1038-1046.

Stoewsand, Gilbert S., Judy L. Anderson, and Richard W. Robinson. "Safety assessment of a nematode-resistant tomato by a simple, short-term rat feeding study." *Regulatory Toxicology and Pharmacology* 24.1 (1996): 6-8.

Chen, Zhang-Liang, et al. "Safety assessment for genetically modified sweet pepper and tomato." *Toxicology* 188.2 (2003): 297-307.

Porrini, Marisa, et al. "Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection." *British Journal of Nutrition* 93.1 (2005): 93-99.

von Oppen-Bezalel, Liki, et al. "The photoprotective effects of a food supplement tomato powder rich in phytoene and phytofluene, the colorless carotenoids, a preliminary study." *Global Dermatol.* 2 (2015): 178-182.

Paetau, Inke, et al. "Carotenoids in human buccal mucosa cells after 4 wk of supplementation with tomato juice or lycopene supplements." *The American journal of clinical nutrition* 70.4 (1999): 490-494.

Müller, H., et al. "Plasma concentrations of carotenoids in healthy volunteers after intervention with carotenoid-rich foods." *European journal of nutrition*38.1 (1999): 35-44.

Appendix A

CERTIFICATE OF ANALYSIS

PhytoflORAL® Pure 0908 Classic

Created by: QA
Effective Date: 28 Mar 2017

Product name	PhytoflORAL® Pure 0908 Classic
Product description	Proprietary tomato powder, uniquely rich in phytoene and phytofluene, the multi-functional colorless carotenoids, sourced from specially selected non-GMO tomato fruit. A raw material for the food and beauty industry.

Composition

Component	%
Solanum lycopersicum (tomato) fruit; dehydrated, powdered	100

CoA No.: 2062/17 **COA Issue Date:** 2017 Aug 02 **Lot No.:** PK16000005-1

Analysis	Specification		Results
Color	Yellow to pale orange		Conform
Odor	Natural tomato scent		Conform
Flavor	Natural tomato taste		Conform
Appearance	Free flowing powder		Conform
Phytoene and Phytofluene Content (UV-spectrophotometry, λ286nm+λ348nm in Ethanol)	Not less than 10 mg/g		11.34 mg/g
Moisture (Karl Fischer)	<6 %		2.47 %
Other chemical analyses*			
*performed periodically			
(ICP, AOAC-986.15)	Lead	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Arsenic	<1.0 ppm	<1.0 ppm
(AA)	Mercury	<0.1 ppm	<0.1 ppm
(ICP, AOAC-986.15)	Cadmium	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Copper	<10 ppm	<10 ppm
Microbial evaluation	Total plate count	<1,000 CFU in 1gr	Conform
	Yeasts/Molds	<100 CFU in 1gr	Conform
	Coliforms	Absent in 1gr	Absent in 1gr
	E. Coli	Absent in 1gr	Absent in 1gr
	Salmonella	Absent in 25gr	Absent in 25gr
	Staph. Aureus	Absent in 1gr	Absent in 1gr
	Ps. Aeroginosa	Absent in 1gr	Absent in 1gr

Storage conditions	Keep in originally sealed package, in a cool and dry place (not exceeding 25°C).
Manufacturing date (YYYY MMM DD)	2017 Jul 23
Expiration date (YYYY MMM DD)	2019 Jan 23

(b) (6)

Dr. Einat Sharon
Head of QC
IBR LTD

IBR PATENTED

4 Faran St., Bldg.10, Yavne Technological Park, Yavne 8122503, ISRAEL, Tel +972-8-9465433, Fax +972-8-9472174, ibroffice@ibrweb.com, www.ibrweb.com

CERTIFICATE OF ANALYSIS

PhytoflORAL® Pure 0908 FINE

Created by: QA
Effective Date: 28 Mar 2017

Product name	PhytoflORAL® Pure 0908 FINE
Product description	Proprietary tomato powder, uniquely rich in phytoene and phytofluene, the multi-functional colorless carotenoids, sourced from specially selected non-GMO tomato fruit. A raw material for the food and beauty industry

Composition

Component	%
Solanum lycopersicum (tomato) fruit; dehydrated, powdered	100

CoA No.: 2036/17 **COA Issue Date:** 2017 Jul 25 **Lot No.:** PK15480006-2

Analysis	Specification		Results
Color	Yellow to pale orange		Conform
Odor	Natural tomato scent		Conform
Flavor	Natural tomato taste		Conform
Appearance	Free flowing powder		Conform
Phytoene and Phytofluene content (UV-spectrophotometry, λ286nm+λ348nm in Ethanol)	Not less than 10 mg/g		14.62 mg/g
Moisture (Karl Fischer)	<6 %		2.88 %
Other chemical analyses*			
*performed periodically			
(ICP, AOAC-986.15)	Lead	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Arsenic	<1.0 ppm	<1.0 ppm
(AA)	Mercury	<0.1 ppm	<0.1 ppm
(ICP, AOAC-986.15)	Cadmium	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Copper	<10 ppm	<10 ppm
Microbial evaluation	Total plate count	<1,000 CFU in 1gr	Conform
	Yeasts/Molds	<100 CFU in 1gr	Conform
	Coliforms	Absent in 1gr	Absent in 1gr
	E. Coli	Absent in 1gr	Absent in 1gr
	Salmonella	Absent in 25gr	Absent in 25gr
	Staph. Aureus	Absent in 1gr	Absent in 1gr
	Ps. Aeroginosa	Absent in 1gr	Absent in 1gr
Storage conditions	Keep in originally sealed package, in a cool and dry place (not exceeding 25°C).		
Manufacturing date (YYYY MMM DD)	2017 Apr 02		
Expiration date (YYYY MMM DD)	2018 Oct 02		

(b) (6)

Dr. Einat Sharon
Head of QC
IBR LTD

IBR PATENTED TECHNOLOGY

4 Faran St., Bldg 10, Yavne Technological Park, Yavne 8122503, ISRAEL, Tel: +972-8-9465433, Fax: +972-8-9472174, ibroffice@ibrweb.com

CERTIFICATE OF ANALYSIS

PhytoflORAL® Pure 0908 FINE

Created by: QA
Effective Date: 28 Mar 2017

Product name	PhytoflORAL® Pure 0908 FINE
Product description	Proprietary tomato powder, uniquely rich in phytoene and phytofluene, the multi-functional colorless carotenoids, sourced from specially selected non-GMO tomato fruit. A raw material for the food and beauty industry

Composition

Component	%
Solanum lycopersicum (tomato) fruit; dehydrated, powdered	100

CoA No.: 1907/17 **COA Issue Date:** 2017 Apr 06 **Lot No.:** PK14640006-2

Analysis	**Specification**		**Results**
Color	Yellow to pale orange		Conform
Odor	Natural tomato scent		Conform
Flavor	Natural tomato taste		Conform
Appearance	Free flowing powder		Conform
Phytoene and Phytofluene content (UV-spectrophotometry, λ286nm+λ348nm in Ethanol)	Not less than 10 mg/g		14.82 mg/g
Moisture (Karl Fischer)	<6 %		2.84 %
Other chemical analyses*			
*performed periodically			
(ICP, AOAC-986.15)	Lead	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Arsenic	<1.0 ppm	<1.0 ppm
(AA)	Mercury	<0.1 ppm	<0.1 ppm
(ICP, AOAC-986.15)	Cadmium	<1.0 ppm	<1.0 ppm
(ICP, AOAC-986.15)	Copper	<10 ppm	<10 ppm
Microbial evaluation	Total plate count	<1,000 CFU in 1gr	Conform
	Yeasts/Molds	<100 CFU in 1gr	Conform
	Coliforms	Absent in 1gr	Absent in 1gr
	E. Coli	Absent in 1gr	Absent in 1gr
	Salmonella	Absent in 25gr	Absent in 25gr
	Staph. Aureus	Absent in 1gr	Absent in 1gr
	Ps. Aeroginosa	Absent in 1gr	Absent in 1gr
Storage conditions	Keep in originally sealed package, in a cool and dry place (not exceeding 25°C).		
Manufacturing date (YYYY MMM DD)	2016 Nov 02		
Expiration date (YYYY MMM DD)	2018 May 02		

(b) (6)

Dr. Einat Sharon
Head of QC
IBR LTD

IBR PATENTED TECHNOLOGY

4 Faran St., Bldg 10, Yavne Technological Park, Yavne 8122503, ISRAEL. Tel +972-8-9465433, Fax. +972-8-9472174. ibroffice@ibrweb.com

Appendix B

PRODUCT IDENTIFICATION

Product name	PhytoflORAL® PURE 0908 FINE
Product description	100% tomato product, dry powder, additives free, solvent free.
Composition	Component: Solanum lycopersicum (tomato) fruit; dehydrated, powdered — 100 %
Packaging	Vacuum-packed in polyethylene bags 150 micron, together with oxygen and moisture absorbers, inside a sealed aluminum laminate bag
Recommended storage conditions until use	In originally sealed packaging, in a cool and dry place (not exceeding 25°C)
Shelf life testing storage conditions	1. Accelerated shelf life = 3M @ 40°C in the product's original packaging 2. Long term shelf life = 18M @ RT, not exceeding 25°C until opened, in the product's original packaging
Methods	Organoleptic evaluation of the color, odor, flow and quantification of the phytoene and phytofluene content by UV spectroscopy*.

*quantifications of biological materials by UV spectroscopy can deviate by up to 15%. Below these values, deviations are not considered significant.

1. ACCELERATED SHELF LIFE

According to figure 1, phytoene & phytofluene levels remain stable at 3M accelerated shelf life storage. The color, odor and flow conform to specifications throughout the storage period.

CONCLUSIONS: PhytoflORAL® PURE 0908 FINE is stable at 3M accelerated shelf life, representative of the 18M long term shelf life.

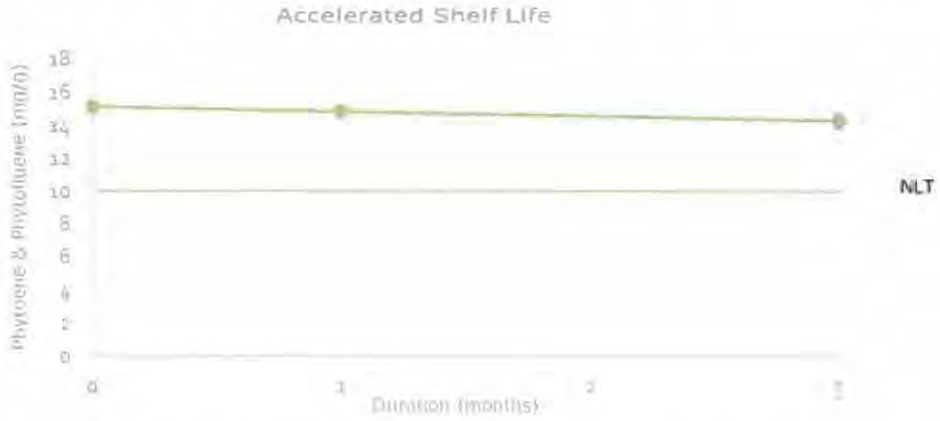

Figure 1 – phytoene & phytofluene carotenoid levels, accelerated shelf life

2. LONG TERM SHELF LIFE

According to figure 2, phytoene & phytofluene levels remain stable at 18M long term shelf life storage. The color, odor and flow conform to specifications throughout the storage period.

CONCLUSIONS: PhytoflORAL® PURE 0908 FINE is stable at 18M shelf life.

Figure 2 – phytoene & phytofluene carotenoid levels, long term shelf life

SUMMARY

PhytoflORAL® PURE 0908 FINE is stable at 18M shelf life as established by accelerated and long term shelf life testing.

NOTES

During use, handling under humid atmosphere conditions should be avoided; where possible we recommend shortening atmosphere exposure times and working under dry or inert atmosphere. End-product packaging should provide an effective oxygen and water barrier (e.g. aluminum laminates), and where possible we recommend packing under dry or inert atmosphere.

The recommendations above are made on the basis of our knowledge of the product. However, recognizing that it is not possible to foresee all possible formulations and processes with our product, we advise our customers to rely on their own internal expertise when processing PhytoflORAL® PURE 0908 FINE into final products, in order to ensure the best result.

(b) (6)

Dr. Einat Sharon
Head of QC