RAMBØLL

ENVIRONMENT
& HEALTH

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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.

RE: GRAS NOTIFICATION FOR CHICORY FLOUR

Dear Sir or Madam:

Date November 29 2018

On behalf of Blue Prairie Brands, Inc., I am pleased to submit this Notification of the Generally Recognized as Safe (GRAS) Determination for Chicory Flour. This Notification contains the expert evaluation report on the GRAS Status of chicory flour prepared by Joseph V. Rodricks, PhD, DABT and Duncan Turnbull, DPhil, DABT of Ramboll US Corporation, who are "experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food" according to the criteria of 21 CFR 170.30.

All of the information supporting the GRAS status of chicory flour cited in this document is publicly available.

Please contact me (703-516-2308; dturnbull@ramboll.com) if you have any questions about this submission.

Yours sincerely

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Prepared for
Blue Prairie Brands, Inc.

Document type
GRAS Notice

Date
November 2018

Generally Recognized as Safe (GRAS) Assessment of Blue Prairie Brands, Inc. Chicory Flour

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1. SIGNED STATEMENTS AND CERTIFICATION

1.1 GRAS Notice Submission

In accordance with 21 CFR Part 170, Subpart E, Ramboll US Corporation (Ramboll), on behalf of Blue Praire Brands, Inc., submits this Generally Recognized as Safe (GRAS) notice to the U.S. Food and Drug Administration (FDA) for "chicory flour." Chicory flour is created from the washing, cooking, dehydration, and grinding of *Cichorium intybus* (commonly known as chicory root), an herbaceous plant of the dandelion family, Asteraceae. The use of chicory flour described herein is exempt from the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for food additives because it is GRAS through scientific procedures and common use in food prior to 1958, as established in Section 201(s) of the FD&C Act and 21 CFR 170.3. The GRAS evaluation has been conducted by Ramboll US Corporation.

1.2 Name and Address of the Submitter

November 29, 2018

Duncan Turnbull, DPhil, DABT
Senior Managing Consultant
Ramboll US Corporation
4350 N. Fairfax Drive, Suite 300
Arlington, VA 22203

On behalf of:

Blue Prairie Brands, Inc,
101 South Hanley Road, Suite 800
St. Louis, MO 63105

1.3 Name of Notified Substance

The subject of this GRAS notification is "chicory flour," also known as "chicory root flour" or "chicory root powder." Chicory flour is created from the washing, cooking, dehydration, and grinding of *Cichorium intybus,* commonly known as chicory root.

1.4 Intended Conditions of Use of the Notified Substance

1.4.1 Food in Which the Substance Will be Used

Blue Prairie Brands intends chicory flour to be used in a variety of foods, including: bakery products (e.g., breads, cookies, cakes, powdered baking mixes, pancake mixes, grain-based bars with or without filling or coating, pizza crusts, waffles); beverages (i.e., carbonated and non-carbonated beverages, wine coolers, water); cereals and other grain products; dairy products and dairy substitutes (e.g., yogurt); desserts (e.g., bulk and novelty ice cream); snacks (e.g., salty snacks such as chips and pretzels); and soups.

1.4.2 Levels of Use in Food

Blue Prairie Brands intends that foods comprised of chicory flour will contain an average of about 6 grams chicory flour per serving. By weight, foods may contain anywhere from 1% to approximately

42% chicory flour, depending on serving size. The levels of use in food are expected to vary by the type of product. For example, crackers that are not typically eaten as snacks (e.g., melba toast, hard bread sticks, ice cream cones, oyster crackers) may contain up to approximately 42% w/w chicory flour, while beverages may contain up to 1% w/w chicory flour.

1.4.3 Purposes for Which the Substance Will be Used

Chicory flour will be used to incorporate inulin into foods. Inulin is a naturally-occurring polydisperse β(2,1) fructan (fructo-oligosaccharide – FOS) that is present in over 36,000 plant species, and which meets FDA's definition of a dietary fiber (FDA, 2016a,b; FDA, 2018; Niness 1999). Foods containing dietary fiber are widely understood to provide health benefits (USDHHS and USDA, 2015; 21 CFR 101.77). Inulin is a GRAS substance (FDA GRAS Notice No. GRN 000118[1]), and the extract of chicory is a GRAS substance (21 CFR 182.20).

Blue Prairie Brands does not expect any specific subpopulations to consume chicory flour.

1.5 Statutory Basis for Conclusion

The use of chicory flour described herein is GRAS through scientific procedures and common use in food prior to 1958, as described below (21 CFR 170.30):

> "(a) General recognition of safety may be based only on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be either (1) scientific procedures or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food."

General recognition of safety requires that "there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use." (21 CFR 170.3(i)).

1.6 Exemption from Premarket Approval Requirements of the FD&C Act

The use of chicory flour described herein is GRAS, and is, therefore, not subject to the premarket approval requirements of Section 409 of the FD&C Act for food additives.

1.7 Availability of Data and Information to FDA

Should FDA ask to see the data and information that are the basis for Ramboll's conclusion of GRAS status, Ramboll and Blue Prairie Brands will...

i) Agree to make the data and information available to FDA;
ii) Agree to the following procedures: Upon FDA's request, Ramboll and Blue Prairie Brands, Inc. will allow FDA to review and copy the data and information as provided in 21 CFR 170.225(c)(7).

1.8 Freedom of Information Act (FOIA)

None of the data and information in Parts 2 through 7 of this GRAS notice is exempt from disclosure under the Freedom of Information Act, 5 U.S.C. 552.

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[1] GRAS Notice 000118 available at https://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices.

1.9 Certifications

To the best of the knowledge of Blue Prairie Brands and Ramboll, this GRAS notice is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to Ramboll and pertinent to the evaluation of the safety and GRAS status of the use of chicory flour in food.

1.10 Name, Position, and Signature of Certifier

Based on an evaluation of relevant data laid out within this report, Ramboll has determined that Blue Prairie Brands' Chicory flour is safe for its intended uses and generally recognized as safe (GRAS) under the terms of 21 CFR 170.30.

We have also concluded that other "experts qualified by scientific training and experience to evaluate the safety of food and food ingredients" would agree.

Joseph V. Rodricks, PhD, DABT

Principal, Ramboll US Corporation

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2. IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS, AND PHYSICAL OR TECHNICAL EFFECT

2.1 Scientific Data and Information that Identifies the Notified Substance

2.1.1 Substance Name, Origin, Composition, and Other Characteristic Properties

Chicory flour is created from the washing, cooking, dehydration, and grinding of *Cichorium intybus* (commonly known as chicory root), an herbaceous plant of the dandelion family Asteraceae. Chicory flour is primarily comprised of carbohydrates (primarily inulin [55-68%], insoluble fiber [14-27%], and sugars [4-6%]), plus protein (4-7%), moisture (8%), minerals, and ash (4%), and fat (1%).

The source of chicory flour, *Cichorium intybus,* is an erect, woody perennial herb that has historical usage spanning back to the time of the ancient Egyptians. The ancient Egyptians are thought to have used *Cichorium intybus* as a medicinal plant, vegetable crop, and animal forage product. Use of *Cichorium intybus* as a foodstuff has continued into recent eras; in 2002, the United States imported over 1.9 million kilograms of roasted chicory root for use as a coffee substitute (Schmidt et al., 2007). Inulin, the primary constituent of chicory, is characterized by its fructose units linked by β(2-1) bonds. Inulin's chain lengths may contain anywhere from 2 to 60 units, with an average degree of polymerization of approximately 10 (Niness 1999).

Chicory flour is a free-flowing off-white flour free of gluten and lactose. Microbially, chicory flour contains <100 cfu/g yeast and mold, a <5,000 cfu/g aerobic plate count, and <100 cfu/g coliforms. Chicory flour imparts a mild flavor. The nutritional content of chicory flour (mean of two recent lots) is presented in Table 1. Individual levels of components may vary within the ranges identified above depending upon culture and storage conditions of the chicory root.

Table 1: Nutrients per 100 Grams Chicory Flour

Basic Components	Quantification
Gram Weight (g)	100
Calories (kcal)	373
Calories from fat	6.5
Calories from Sat Fat	2
Protein (g)	6
Carbohydrates (g)	86
Total Dietary Fiber (g)	81
Soluble Fiber (g)	58
Insoluble Fiber (g)	24
Total Sugars (g)	5
Fat (g)	1
Saturated Fat (g)	0
Trans Fatty Acid (g)	0
Cholesterol (mg)	0
Water (g)	4
Source: Blue Prairie Brands, Inc.	

2.2 Information Identifying Biological Material

2.2.1 Taxonomic Source

Included below is the taxonomic information for *Cichorium intybus*, the source of chicory flour.

Kingdom: Plantae
Phylum: Angiosperms
Division: Eudicots
Class: Asterids
Order: Asterales
Family: Asteraceae
Genus: *Cichorium*
Species: *C. intybus*

Blue Prairie Brands intends to use the "Chrysolite" variety of *Cichorium intybus*, which is a low bitter chicory plant. According to a taste test conducted by Blue Prairie Brands, chicory flour made using the "Chrysolite" variety is less bitter than chicory flour using the "Orchies" variety (US Patent Application No. 14/875,093). The difference in bitterness is attributable to differences in sesquiterpene lactones; the "Chrysolite" variety of *Cichorium intybus* contains fewer sesquiterpene lactones than other varieties of *Cichorium intybus*, including "Orchies" (US Patent Application No. 14/875,093).

2.2.2 Part of Plant Used as Source

Blue Prairie Brands intends to use the taproot of *Cichorium intybus*.

2.2.3 Known Toxicants Present in the Source

Case reports have reported inhalative, oral, and/or cutaneous allergic symptoms following exposure to *Cichorium intybus*, primarily within occupational settings (Cadot et al., 1996; Cadot et al., 2003; Helbling et al., 1997; Morita et al., 2007; Nemery et al., 1989; Pirson et al., 2009). Blue Prairie will not be selling chicory flour as a powder for use in the home and occupational exposure for workers can be limited by education and GMP.

To Ramboll's knowledge, exposure to or consumption of *Cichorium intybus* does not otherwise cause toxic effects in exposed populations. A 28-day toxicity study of male and female Sprague-Dawley rats identified no treatment-related toxic effects from oral chicory root extract consumption of 70, 350, or 1,000 mg/kg/day (Schmidt et al., 2007).

2.2.4 Method of Manufacture

Broadly, the manufacture of Blue Prairie Brands chicory flour requires the following steps:

1) Harvesting and washing of fresh *Cichorium intybus* roots. Chicory variety "Chrysolite" will be planted, grown, and harvested. Following the harvest, intact *Cichorium intybus* are washed and sliced.
2) Cooking of the *Cichorium intybus* roots. Cooking will involve heating the plant material in the presence of exogenous water (i.e., pot of water, steam).

3) Dehydration of fresh *Cichorium intybus* roots. Dehydration may use a wide variety of drying methods including fluidized bed dryer, drum dryer, roasting drum dryer, conventional freeze-drying methods, and/or a conventional microwave. The time and temperature of the drying will be adjusted to achieve a moisture content of less than 10%.

4) Milling the cooked *Cichorium intybus* roots into flour. Milling will involve grinding, cutting, and/or crushing of the cooked *Cichorium intybus* roots using current milling technologies commonly used for food processing.

All of these processes and the equipment used are typical of those used commercially for processing other food types.

2.2.5 Specifications for Food-grade Material

The chicory flour produced by Blue Prairie Brands meets the FD&C Act definition of a "food" and is created using Current Good Manufacturing Practices (CGMP). Information from a May 1, 2017 Certificate of Analysis for chicory flour is provided in Table 2.

Table 2: Information from a May 1, 2017 Certificate of Analysis for Blue Prairie Brands, Inc. Chicory Flour

Characteristic	Results	Method
Color	Cream to beige	Internal visual examination
Flavor	Mild	Internal panel
Moisturei%	5.26%	AOAC: 945.23, 934.01 (modified)
Total Fiber %	77.8%	AOAC: 2011.25
Aerobic Plate Count	<50 cfu/g	FDA BAM Ch. 3
Coliform	<10 cfu/g	AOAC 991.14
Salmonella	Negative/25 g	AOAC RI 031201
Yeast	<10 cfu/g	FDA BAM Ch. 18
Mold	<10 cfu/g	FDA BAM Ch. 18
E. Coli	Negative/1 g	AOAC 991.14
Aflatoxin	<0.500 ppb	MLL
Shelf Life	Min 12 months at <30P C	
cfu: colony-forming units; g: gram; ppb: parts per billion		

2.2.6 Physical or Technical Effect

Chicory flour will be used to incorporate inulin into foods. Inulin is a naturally-occurring, polydisperse β(2,1) fructan that meets FDA's definition of a dietary fiber. Blue Prairie Brands intends that foods comprised of chicory flour will contain an average of 6 grams chicory flour per serving. By weight, foods may contain anywhere from 1% to approximately 42% chicory flour. Blue Prairie Brand's expectations for chicory flour consumption align with mean fiber intake estimates in the United States (see Section 3).

3. DIETARY EXPOSURE

3.1 Estimate of Dietary Exposure to the Notified Substance

Blue Prairie Brands chicory flour primarily contains inulin (soluble fiber) and insoluble fiber. These two constituents represent 55-68% and 14-27% of the chicory flour's composition, respectively. Given that both inulin and insoluble fiber meet FDA's definition of "dietary fiber," this section focuses on how the intended intake of Blue Prairie Brands chicory flour compares to usual intakes of dietary fiber within the United States. This section also attempts to explain how Blue Prairie Brands chicory flour may help U.S. children, adolescents, and adults, meet recommended intakes of dietary fiber.

Blue Prairie Brands intends that foods made with chicory flour will contain an average of 6 grams of chicory flour per serving, providing approximately 5 grams of dietary fiber per serving. By weight, foods may contain anywhere from 1% to approximately 42% chicory flour. The levels of use in food are expected to vary by the type of product; for example, crackers that are not typically eaten as snacks (e.g., melba toast, hard bread sticks, ice cream cones, oyster crackers) may contain up to approximately 42% w/w chicory flour, while beverages may contain up to 1% w/w chicory flour.

3.1.1 Adequate Intakes of Dietary Fiber for U.S. and Canadian Populations

The Food and Nutrition Board of the National Academies of Sciences, Engineering, and Medicine (NASEM) have determined "adequate intakes" of fiber for U.S. and Canadian populations to range from 19 grams/day (for children ages 1-3 years old) through 38 grams/day (for men ages 14-50 years old) (NASEM 2002). Table 3 includes a summary of NASEM's adequate intake levels for "Total Fiber" by life stage group and NASEM's related commentary.

Table 3: Dietary Reference Intakes and Related Commentary for Adequate "Total Fiber" Intakes, as Presented by NASEM (2002)

Function	Life Stage Group	Adequate Intake Level (grams/day)	Selected Food Sources	Adverse Effects of Excessive Consumption
Improves laxation, reduces risk of coronary heart disease, assists in maintaining normal blood glucose levels.	**Infants**		Includes dietary fiber naturally present in grains (such as found in oats, wheat, or unmilled rice) and functional fiber synthesized or isolated from plants or animals and shown to be of benefit to health.	Dietary fiber can have variable compositions and therefore it is difficult to link a specific source of fiber with a particular adverse effect, especially when phytate is also present in the natural fiber source. It is concluded that as part of an overall healthy diet, a high intake of dietary fiber will not produce deleterious effects in healthy individuals. While occasional adverse gastrointestinal symptoms are observed when consuming some isolated or synthetic fibers, serious chronic adverse effects have not been observed. Due to the bulky nature of fibers, excess consumption is likely to be self-limiting. Therefore, a UL [upper limit] was not set for individual functional fibers.
	0-6 months	ND		
	7-12 months	ND		
	Children			
	1-3 years	19		
	4-8 years	25		
	Males			
	9-13 years	31		
	14-18 years	38		
	19-30 years	38		
	31-50 years	38		
	50-70 years	30		
	>70 years	30		

Function	Life Stage Group	Adequate Intake Level (grams/day)	Selected Food Sources	Adverse Effects of Excessive Consumption
	Females			
	9-13 years	26		
	14-18 years	26		
	19-30 years	25		
	31-50 years	25		
	50-70 years	21		
	>70 years	21		
	Pregnancy			
	≤ 18 years	28		
	19-30 years	28		
	31-50 years	28		
	Lactation			
	≤ 18 years	29		
	19-30 years	29		
	31-50 years	29		
ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.				

3.1.2 Estimated/Actual Intakes of Dietary Fiber for U.S. Populations

A study utilizing U.S. National Health and Nutrition Examination Survey (NHANES) data estimates the ten-year trends in the fiber intakes of U.S. populations from various food sources (McGill et al., 2015)i Using data from 2001 through 2010, McGill and colleagues estimate that children and adolescents (ages 4-18 years) consumed an average of 13.2 grams fiber/day from all food sources, while adults (ages 19 years and older) consumed an average of 16.1 grams fiber/day from all food sources. The greatest sources of fiber in children's diets included "grains/mixtures/frozen plate meals/soups/meat substitutes/dry beans/peas/legumes/nuts and seeds" (contributing 2.3 grams/day), vegetables (2.1 grams/day), and "all other foods" (1.9 grams/day). The greatest sources of fiber in adults included vegetables (contributing 3.4 grams/day), "all other foods" (2.1 grams/day), fruits (2.0 grams/day) and "grains/mixtures/frozen plate meals/soups/meat substitutes/dry beans/peas/legumes/nuts and seeds" (2.0 grams/day). These intake levels fall far short of the intake levels recommended by NASEM (2002)i Table 4 presents a summary of relevant data reported in the study by McGill and colleagues.

Table 4: Ten-year Trends in Fiber Food Sources for Children/Adolescents (4-18 Years Old) and Adults (Ages 19 years and Older), McGill et al., 2015

Children/Adolescents (n=14,973)		
Food Category	**Mean 2001-2010 Intake (grams/day)**	**Mean % Fiber Contribution**
Yeast breads/rolls	1.2	10.5
Quick breads	0.4	2.7
Cakes/cookies/pies/pastries	0.6	5.2
Crackers and salty grain snacks	0.9	6.9
Pancakes/waffles/French toast/crepes	0.2	2.0
Pastas	0.08	0.6
Hot cereals/rice	0.2	1.4
RTE cereals	0.9	6.3
Grain mixtures/frozen plate meals/soups/meat substitutes	2.3	16.3
Dry beans/peas/legumes/nuts and seeds	0.8	4.4
Fruits	1.6	11.3
Vegetables	2.1	16.6
All other foods	1.9	15.8
Total	**13.2**	**100**
Adults (n=24,809)		
Food Category	**Mean 2001-2010 Intake (grams/day)**	**Mean % Fiber Contribution**
Yeast breads/rolls	1.6	11.9
Quick breads	0.6	3.4
Cakes/cookies/pies/pastries	0.6	4.3
Crackers and salty grain snacks	0.7	4.6
Pancakes/waffles/French toast/crepes	0.1	0.9
Pastas	0.09	0.5
Hot cereals/rice	0.4	2.3
RTE cereals	0.9	4.8
Grain mixtures/frozen plate meals/soups/meat substitutes	2.0	12.0
Dry beans/peas/legumes/nuts and seeds	1.6	7.2
Fruits	2.0	11.1
Vegetables	3.4	22.6
All other foods	2.1	14.3
Total	**16.1**	**100**

3.1.3 Reconciliation of Adequate Intakes and Estimated/Actual Intakes of Dietary Fiber

The Food and Nutrition Board of the National Academies of Sciences, Engineering, and Medicine (NASEM) have determined "adequate intakes" of dietary fiber to range from 25-38 grams/day for children and adolescents ages 4 to 18 years old, and 21-38 grams/day for adults ages 19 and older. However, actual intakes in U.S. populations from 2001 to 2010 do not meet these recommendations; during this time, children and adolescents consumed an average of 13.2 grams fiber/day from all food sources, while adults consumed an average of 16.1 grams fiber/day from all food sources. On

average, children and adolescents could consume up to 5 additional servings of chicory flour-based products (at 5 grams dietary fiber/serving) to meet NASEM's adequate intake recommendations. Adults could consume up to an average of 4 additional servings of chicory flour-based products (also at 5 grams dietary fiber/serving) to meet the same recommendations. Among other foods, Blue Prairie Brands intends that chicory flour will be incorporated into conventional flour-based foods that otherwise represent relatively poor sources of dietary fiber in the U.S. diet (Table 4). The substitution of chicory flour for conventional flour in such products could help U.S. children, adolescents, and adults meet NASEM's recommended adequate intakes for dietary fiber.

3.2 Dietary Exposure to Other Substances Expected to be Formed in or on Food

The intended use of chicory flour will not expose populations to other substances formed in or on food. For example, the intended use of chicory flour will not generate hydrolytic products or reaction products within foods.

3.3 Dietary Exposure to Other Substances Present in the Notified Substance

The intended use of chicory flour will not expose populations to known contaminants or by-products. Chicory flour is created using *Cichorium intybus* roots, exogenous water, and heat; manufacture of chicory flour does not utilize additional chemical processing aids or substances other than those commonly used for similar processing of other food types. For example, sodium pyrophosphate is used as a processing aid in the drying phase of the production of chicory flour, just as it is in the production of dried potato pieces. Sodium pyrophosphate is a GRAS sequestrant (its purpose in this case is to prevent discoloration of the chicory root) with no restriction on conditions of use other than "in accordance with good manufacturing practice" (21 CFR 182.6787). No significant increase in human exposure to sodium pyrophosphate is anticipated. As described in Section 2.2.3, consumption of *Cichorium intybus* does not cause toxic reactions in humans, beyond occasional reports of individuals' allergic symptoms.

3.4 Data Sources and Assumptions

Data relied upon within this section include chicory flour usage estimates provided to Ramboll by Blue Prairie Brands; the adequate intake recommendations of NASEM (2002); and information from an analysis of publicly-available NHANES data (McGill et al., 2015). Ramboll relied upon mean chicory flour usage estimates to drive the safety evaluation. However, as described in the next section, consumption of chicory flour is self-limiting due to the high levels of dietary fiber present.

4. SELF-LIMITING LEVELS OF USE

Blue Prairie Brands chicory flour primarily contains inulin and insoluble fiber. These two constituents represent 55-68% and 14-27% of the chicory flour's composition, respectively. Given that both inulin and insoluble fiber meet FDA's definition of "dietary fiber," this section focuses on the self-limiting levels of dietary fiber and inulin consumption.

The benefits and potential effects of dietary fiber consumption have been widely studied and were considered in NASEM's evaluation of a dietary reference intake for total fiber (NASEM 2002). Considering dietary fibers alongside other fibers, NASEM concludes:

> "While occasional adverse gastrointestinal symptoms are observed when consuming some of the isolated or synthetic fibers, serious chronic adverse effects have not been observed. Furthermore, due to the bulky nature of fibers, excess consumption is likely to be self-limiting. Therefore, a UL [Tolerable Upper Intake Level] was not set for these individual fibers." (NASEM 2002)

Within their more specific consideration of inulin, oligofructose, and fructooligosaccharide, NASEM reports, "cramping, bloating, flatulence, and diarrhea was observed at intakes ranging from 14 to 18 g/d [grams/day] of inulin" within studies of inulin consumption (NASEM 2002). These short-term and reversible effects are likely to limit individuals from consuming excessive amounts of dietary fiber via chicory flour.

5. GRAS BASED ON COMMON USE IN FOOD BEFORE 1958

Cichorium intybus has been substantially consumed safely as a foodstuff for millennia. The ancient Egyptians used *Cichorium intybus* as a medicinal plant, vegetable crop, and animal forage product (Schmidt et al., 2007; Wang and Cui, 2011), and the ancient Greeks and Romans also grew it as a vegetable crop; its use was mentioned by several ancient writers including Horace, Virgil, Ovid, and Pliny the Elder (Grieve, 1971; Wang and Cui, 2011).

During the 18th, 19th, and 20th centuries, Western societies used *Cichorium intybus* root extract, or roasted and ground roots as a coffee substitute, particularly during times of financial hardship (e.g., the Napoleonic wars, the Great Depression, and World War II) (Kandeler and Ullrich, 2009). Coffee mixed with or using *Cichorium intybus* root extract gained popularity in the United States particularly during the American Civil War (1861-1865) (Smithsonian Magazine, 2014). That article points to the history of the addition of chicory to coffee that continues to this day, particularly in New Orleans, that dates from the Civil War period when Union naval blockades cut off coffee imports into New Orleans at a time when it was the second largest importer of coffee in the United States, and coffee drinkers in the area normally supplied through New Orleans were required to add roasted chicory root to stretch their diminishing supply of coffee. This use continued even after the Civil War, and continues to this day.

References to the use of chicory as food, particularly when added to coffee, have appeared in newspapers throughout the United States for more than 150 years (see for example: New York Herald, 1851; Hillside Standard, 1864; Washington Register, 1892; Sioux City Journal, 1897; Willmar Tribune, 1897; Birmingham Times, 1908; River Press, 1909; Chicago Tribune 1926; Alexandria Daily Town Talk, 1929; Chicago Tribune, 1941). The 1851 entry in the New York Herald, cited above, for example, was an advertisement offering chicory root, chicory meal (i.e., chicory flour), and chicory cakes for sale. Several of the other historical newspaper articles cited above extolled the benefits of chicory root in various forms, and foods made from it. An article in the Birmingham Times (Alabama) in 1908 described the use of chicory in coffee and noted that "the United States government has interested itself in the root and recently issued a bulletin on the use and growth of chicory. (See Bulletin 19, U.S. Department of Agriculture)." An article in the Chicago Tribune in 1941 described the use of ground chicory root in coffee, and also recommended a recipe for Macaroni with Chicory Sauce, that used chicory root powder.

An article in the Washington Register (Kansas) in 1892 reported that the US was importing $8,000,000-worth of chicory from Germany at that time. The article noted that its wholesale price at that time was 12c/pound, indicating that more than 60 million pounds of chicory was being imported for consumption in the US in 1892. An article in the Chicago Tribune in 1926 reported that practically all of the chicory grown in the United States was grown in Michigan for use with coffee, and the total annual production of chicory was about 58,500 tons (117 million pounds). An article in the Port Huron Times Herald (1954) reported a somewhat lower consumption at that time, noting that "national consumption of chicory in 1953 was about 12 million pounds. Michigan produced about four million pounds, and the rest was imported from Belgium, Holland and Poland."

These citations document the broad availability and consumption of chicory root throughout the United States for more than 150 years.

Use of *Cichorium intybus* root extract as a foodstuff has continued into the modern era; in 2002, the United States imported over 1.9 million kilograms of roasted chicory root for use as a coffee substitute (Schmidt et al., 2007).

Based on this extensive history of varied food uses of chicory in various forms, including as meal or flour, chicory flour is GRAS.

6. NARRATIVE

6.1 Explanation of Basis for GRAS Determination of Blue Prairie Brands Chicory Flour

When consumed as intended, Ramboll concludes that the chicory flour produced by Blue Prairie Brands meets FDA's requirements for a GRAS substance, based both on scientific procedures and common use in food prior to 1958. Chicory flour is made from the taproot of *Cichorium intybus*, the extract of which is listed as a GRAS substance within FDA's list of GRAS "essential oils, oleoresins (solvent-free), and natural extractives (including distillates)." Chicory flour is comprised primarily of inulin (55-68%) and insoluble fiber (14-27%), both of which are considered "dietary fiber" by FDA, and the former of which is considered GRAS by FDA.[2] Inulin is a fructo-oligosaccharide (FOS), characterized by β 2,1 linkages of fructose monomers, generally with a single terminal glucose molecule. The degree of polymerization (DP) ranges from 2 to 60 (GRN-118). Extensive data summarizing the lack of toxicity and demonstrating the safety of chicory root, inulin, and related fructo-oligosaccharides are summarized in those GRAS Notices.[2] As noted in Section V.D (pp. 55-58) of GRN-118:

> "there have been extensive animal tests on inulin to determine both metabolism and tolerance. No untoward effects were seen in these studies when dose levels have ranged from 10 to 25 percent inulin in the diet for 3 to 4 weeks or 5 to 20 percent of FOS (DP≤ 8) in the diet for up to 5 weeks. Results from subchronic and chronic toxicity and carcinogenicity studies in rats (Tokunaga, Oku, and Hosoya 1986; Clevenger et al. 1988) demonstrate that there are no significant adverse effects up to 2,170 mg/kg/day. The no-observed effect level (NOEL) for chronic administration of Neosugar®-brand inulin fructo-oligosaccharide is 2,170 mg/kg/day. The only effect noted was the occurrence of soft stools or diarrhea after ingestion of large quantities of Neosugar (more than 5 percent in the diet of rats).
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> "Carabin and Flamm (1999) evaluated the safety of inulin and oligofructose and concluded that results from toxicology tests on inulin-type fructans have not shown evidence of mortality, morbidity, target organ toxicity, reproductive or developmental toxicity, mutagenicity or carcinogenicity. These authors concluded that inulin-type fructans are safe for human consumption under intended conditions of use and that up to 20 g/day of inulin and/or oligofructose is well tolerated."

An absence of adverse effects was also seen in a 28-day toxicity study of male and female Sprague-Dawley rats ingesting chicory root extract at 70, 350, or 1,000 mg/kg/day (Schmidt et al., 2007).

Section V.D of GRN-118 also reports a lack of genotoxic potential of Neosugar® brand FOS in a battery of test systems in bacteria and mammalian cells, and there were no significant adverse effects or carcinogenic potential after chronic administration of up to 2,170 mg/kg/day (Clevenger et al. 1988). The gastrointestinal effects (diarrhea and enlarged cecum) noted in animal studies are consistent with the gastrointestinal disruptions caused by high levels of similar non-digestible materials, as reported by Carabin and Flamm (1999).

Soluble and insoluble dietary fiber, like that in chicory flour, is considered beneficial to health by the U.S. Department of Health and Human Services, and do not require a Tolerable Upper Intake Level (UL) due to their self-limiting effects (USDHHS and USDA, 2015; 21 CFR 101.77; NASEM 2002). When produced in accordance with CGMP, the manufacture of chicory flour does not significantly alter the dietary fiber-related health benefits of *Cichorium intybus* consumption, nor does such manufacture introduce additional non-*Cichorium intybus* substances into the human diet.

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[2] GRAS Notice 000118 (Inulin) and 000477 (Long-chain inulin) available at https://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices

As noted in Section V.E of GRN-118, aside from gastrointestinal effects common to high intake levels of non-digestible carbohydrates, the only adverse health effect that has been identified with chicory are associated with occupational dermal and possibly inhalation exposure. According to Warshaw and Zug (1996), the reactions that have been observed are of three types: eczematous contact dermatitis of the hands and forearms, contact urticaria, or seasonal photodermatitis-like eczematous rash of the arms, face and neck. In addition, two case reports indicated that chicory exposure was associated with an immediate-type allergy in a green grocer and occupational asthma in a market gardener. This allergic response is due to the sesquiterpene lactones that occur in chicory, and also in many other plants of the Asteraceae (formerly Compositae) family, many of which, including sunflowers, chrysanthemums, lettuce, and artichokes, cause similar allergic reactions in some individuals (Warshaw and Zug 1996; Crawford 2016). All of these finding relate to exposure to the intact raw plant, and would not be expected to occur with the processed chicory flour.

In Section V.F (pp. 60-67) of GRN-118, more than 20 clinical trials are summarized with exposures lasting from a few days to one year and evaluating human tolerance to inulin. The only adverse effects reported in these studies were some cases of flatulence and diarrhea, particularly at very high daily doses (160-200 g/day). The authors of that GRAS Notice concluded:

> "Based on the clinical studies reviewed, no adverse effects have been associated with the repeated consumption of inulin in amounts up to approximately 70 grams per day. At consumption levels above 70 grams of inulin per day, intestinal gas formation, diarrhea, and other gastrointestinal disorders associated with high fiber intake were shown to occur."

Additional data supporting the safety of inulin and chicory root are reported in GRN-477. That includes the results of thirteen clinical trials involving the administration of infant formulas containing added nondigestible carbohydrates comprised of 90% galacto-oligosaccharides (GOS) and 10% FOS (long-chain inulin) to preterm infants (GRN-477, section 5.8). This mixture was well tolerated by the infants, and no adverse effects were observed on measures of growth, fluid balance, formula intake, or stool characteristics. This mixture was also well tolerated in 43 clinical trials in term infant formulas and weaning foods (GRN-477, section 5.7.2). Long-chain inulin, with or without added oligofructose or GOS was also well tolerated in four clinical trials in adults (GRN-477, Table 5-3, p. 33).

6.2 Availability of Data and Certifying Statements

All of the information reviewed by Ramboll as part of this safety evaluation are publicly available, and listed in Section 7.

The information reviewed by Ramboll and described within this Notice provide the basis for Ramboll's conclusion that Blue Prairie Brands, Inc. chicory flour is generally recognized among qualified experts to be safe under the conditions of its intended use.

Ramboll has reviewed all available data and information, and is not aware of any data or information that are, or may appear to be, inconsistent with Ramboll's conclusion of GRAS status.

All of the safety-related data reviewed herein by Ramboll are generally available to the public and none is exempt from disclosure under the Freedom of Information Act.

7. LIST OF SUPPORTING DATA AND INFORMATION

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