**PART 7. §170.255. LIST OF SUPPORTING DATA AND INFORMATION**

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# Expert Panel Consensus Statement Concerning the Generally Recognized as Safe (GRAS) Status of *Clostridium* Protein for Use in Foods

## INTRODUCTION

Superbrewed Food, Inc. (hereafter referred to as "Superbrewed Food") convened a panel (the "Expert Panel") of independent scientists, qualified by their scientific training and relevant national and international experience to evaluate the safety of food ingredients, to conduct a critical and comprehensive evaluation of the available pertinent data and information on *Clostridium* protein, and to determine whether the intended uses of *Clostridium* protein in specified conventional food and beverage products would be Generally Recognized as Safe (GRAS) based on scientific procedures. The food uses of *Clostridium* protein include meat and poultry analogs, dairy analogs, prepared meals, meal replacement products, milk and non-milk-based nutritional beverages, vegetable and fruit-based drinks, baked goods, breakfast cereals, soups, dressings and sauces at levels ranging from 1 to 40% by weight of the ready-to-eat (RTE) or ready-to-drink (RTD) products. In protein powders for formulation into beverages using milk or water for consumption as a supplemental protein source in the diet, use levels will vary up to a maximum of 90% by weight in the powder. The Expert Panel consisted of the below-signed qualified scientific experts: Professor Eric Johnson (University of Wisconsin-Madison), Professor Kelly Swanson (University of Illinois at Urbana-Champaign) and Dr. Ashley Roberts (AR Toxicology, Inc.).

The Expert Panel, independently and collectively, critically evaluated a comprehensive package of scientific information and data. This information was presented in a dossier provided by Superbrewed Food [Documentation to Support the Generally Recognized As Safe (GRAS) Status of *Clostridium* Protein for Use in Foods], which included an evaluation of all available scientific data and information, both favorable and unfavorable, relevant to the safety of *Clostridium* protein for the intended food uses. The body of data was prepared in part from a comprehensive search of the scientific literature and also included information characterizing the source and identity of the ingredient, manufacture of the ingredient, product specifications, supporting analytical data, stability data, intended conditions of use, estimated exposure under the conditions of intended use, potential allergenicity and *in vitro* digestibility, as well as studies evaluating the safety of the ingredient. In addition, the Expert Panel evaluated other information deemed appropriate or necessary.

Following independent critical evaluation, the Expert Panel unanimously concluded that *Clostridium* protein, manufactured consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate food-grade specifications, is GRAS based on scientific procedures, under the conditions of intended use in specified conventional foods and beverages as described above. A summary of the basis for the Expert Panel's conclusion appears below.

**SUMMARY AND BASIS FOR GRAS**

Superbrewed Food intends to market *Clostridium* protein for use as a direct protein replacement of animal-, fungal- or vegetable-based protein currently used in foods and beverages in the United States (U.S.), and as a supplement to the protein occurring naturally in existing food products. *Clostridium* protein is an off-white powder comprising the dried killed cells obtained from *Clostridium tyrobutyricum* fermentation using a corn-derived sugar feedstock.

The microbial source has been unambiguously characterized as the non-spore forming *C. tyrobutyricum* ASM#19. Whole Genome Sequence (WGS) analysis indicates the absence of any genetic element sequences that code for virulence factors or protein toxins. Phenotypic and WGS analysis together indicate that the strain has not acquired any antimicrobial resistance and is susceptible to antimicrobials of human and veterinary importance. Testing for inhibitory activity of culture supernatants against reference strains also confirms *C. tyrobutyricum* ASM#19 does not produce antimicrobial substances. Consistent with the cells from the fermentation being killed during the manufacturing process, only low levels of viable cells were detected in 5 representative lots of *Clostridium* protein, with levels ranging from 160 to 2,390 CFU/mL.

The raw materials and processing aids used in the commercial production of *Clostridium* protein are food-grade and permitted for use in food. The manufacturing processing involves (1) grinding and liquefaction of corn; (2) further processing of liquefied corn to yield one of two possible feedstocks, referred to as “Clear Sugar” and “Clear Mash”, respectively; (3) anaerobic fermentation using *C. tyrobutyricum* ASM#19; and (4) separation, washing and drying of the killed cells to yield *Clostridium* protein. A heat-treatment step (70°C for 20 minutes) is included in the production process to reduce the nucleic acid levels in *Clostridium* protein to no more than 4 g/100 g. Commercial production of *Clostridium* protein will be in accordance with cGMP and a Hazard Analysis Critical Control Point (HACCP) plan will be in place. The process will also comply with the requirements of the Food Safety and Modernization Act (FSMA).

Appropriate food-grade specifications are established for *Clostridium* protein which include well-defined ranges for the levels of the primary nutrient (protein) and compositional components of potentially toxicological concern (nucleic acids and ammoniacal N). Criteria to control the levels of heavy metals and microbiological contaminants are also included. The results of analysis for 5 lots of *Clostridium* protein considered representative of the commercial material verify that the ingredient can be manufactured in conformance with the compositional and contaminant specifications, and that acceptable lot to lot variability can be achieved. *Clostridium* protein comprises a minimum of 80 g/100 g of protein and maximum of 3 g/100 g of fat, 5 g/100 g of carbohydrates, 6 g/100 g of ash and 10 g/100 g of moisture. The amino acid composition, mineral content and vitamin profile of *Clostridium* protein were also determined analytically. Further analysis revealed that only low levels of residual fermentation metabolites (organic acids and 2,3-butanediol) were present in *Clostridium* protein after separation of the cells. No biogenic amines were identified at amounts which might pose a safety concern and the absence of any detectable levels of mycotoxins was confirmed.

A stability study is ongoing to establish a shelf-life for *Clostridium* protein stored unopened in the original packaging at ambient temperature (<25°C) in the absence of excessive moisture or direct

sunlight. The interim results of the study showed that storage of *Clostridium* protein for 3-months at 25°C and 60% relative humidity (RH) in bags representative of the commercial packaging, was not associated with any detrimental changes in organoleptic properties, composition, microbiological parameters or levels of biogenic amines.

The food uses of *Clostridium* protein include meat and poultry analogs, dairy analogs, prepared meals, meal replacement products, milk and non-milk-based nutritional beverages, vegetable and fruit-based drinks, baked goods, breakfast cereals, soups, dressings and sauces at levels ranging from 1 to 40% by weight of the RTE or RTD products. In protein powders for formulation into beverages using milk or water for consumption as a supplemental protein source in the diet, use levels will vary up to a maximum of 90% by weight in the powder. Under the proposed conditions of use, male teenagers were determined to have highest mean and 90$^{th}$ percentile consumer-only intakes of *Clostridium* protein on an absolute basis, at 14.7 and 33.2 g/person/day, respectively. On a body weight basis, infants and young children were identified to have the highest mean and 90$^{th}$ percentile consumer-only intakes of 600 and 1,370 mg/kg body weight/day, respectively.

Comparison of the estimated consumer-only intakes of *Clostridium* protein with the Recommended Daily Allowances (RDAs) for protein for different life stage groups, as well as consumption estimates for protein intakes in practice by the U.S. population (Berryman *et al*., 2018), indicates that the ingredient has the potential to represent a substantive fraction of the daily protein requirements for individuals. In practice, *Clostridium* protein will be a direct replacement for animal-, fungal- and vegetable-based proteins such as *Fusarium* protein (or mycoprotein), casein and pea protein in the diet, and therefore, the ingredient will contribute to, but not alter, the total daily protein intakes from all sources by the U.S. population.

A weight of evidence approach can be applied to support the safety of *Clostridium* protein for the intended use as an ingredient in conventional foods and beverages, based on the following: (1) characterization data on the source microorganism; (2) compositional and *in vitro* digestibility data; (3) comparison of the amino acid sequence of the protein to other proteins known to be allergenic; and (4) toxicological testing using Superbrewed Food's product.

Assessment of the safety of the source microorganism can largely be based on the Pariza *et al*. (2015) decision tree for microbial cultures. Although the guidelines are primarily envisaged to assess the safety of microbial cultures for use in fermented food and feed production, or for probiotic use, the principles and concepts described therein can be applied to *C. tyrobutyricum* as a protein source. One notable difference between microbial cultures for the production of fermented foods or probiotics, and those used as protein sources, is the absence of viable cells in the food ingredient. Thus, elements of the decision trees developed by Pariza and Johnson (2001) and Pariza and Cook (2010) for the assessment of enzyme preparations, which rarely contain viable cells from the source, can be applied to *Clostridium* protein.

*C. tyrobutyricum* occurs naturally in dairy products. There are no reports in the published literature associating *C. tyrobutyricum* with toxin production or pathogenicity in humans or animals. The findings of the genome-wide analysis and physiological evaluation of *C. tyrobutyricum* ASM#19 are consistent with the published literature in which no reports of the species being associated with pathogenicity or

toxigenicity in humans or animals were identified. Taken together, it may be concluded that *C. tyrobutyricum* ASM #19 does not pose a safety concern when used in the manufacture of *Clostridium* protein for use as a food ingredient.

The quality of a protein varies between sources and is principally defined by its amino acid composition and digestibility (Institute of Medicine; IOM. 2019). Besides the protein content, the nutritional value of *Clostridium* protein is also affected by its chemical composition (i.e., nucleic acids, minerals, vitamins and organic acids contents). Comparison of the amino acid profile of *Clostridium* protein with FAO reference values indicates that the ingredient will contribute to, but not adversely impact, essential amino acid intakes from the diet under the conditions of intended use as a direct replacement for animal- and vegetable-derived protein. The *in vitro* digestibility of *Clostridium* protein was high at 96.4% and the % PDCAAS was 75 based on the reference pattern for 2 to 5 year old children (FAO, 1991), 81 based on the updated reference pattern for young children, and 101 based on the updated reference pattern for older children, adolescents and adults (FAO, 2013). Taken together, these data indicate that *Clostridium* protein is a good quality protein source that is not expected to be nutritionally disadvantageous when used as a direct replacement for existing animal-, fungal- and vegetable-based proteins in the specified range of conventional foods and beverages.

An important safety consideration in the production of microbial proteins is the high nucleic acid content and the potential elicitation of gout and kidney stones due to the ingestions of purine compounds from the breakdown of ribonucleic acid (RNA) in the gastrointestinal (GI) tract which increases uric acid concentrations in the blood (PAG, 1974; Gieseke *et al*., 1982; Jonas *et al*., 2001). Nucleic acids occur widely in vegetable-, fungal- and animal-derived foods with typical servings of calf liver, chestnut mushrooms and broccoli estimated to provide in the region of 0.49, 0.23 and 0.72 g/serving, respectively. By comparison, a typical serving of non-dairy cheese containing 20% *Clostridium* protein will provide up to 0.24 g/serving which is in the region of that of a serving of broccoli.

Under the proposed conditions of use of *Clostridium* protein, the highest mean and 90$^{th}$ percentile consumer-only intakes were estimated to be 14.7 and 33.2 g/person/day, respectively. These intakes equate to a nucleic acids exposure of 0.59 and 1.33 g/person/day, respectively for *Clostridium* protein containing the maximum amount of nucleic acids of 4 g/100 g. In terms of overall contribution, similar to other microbial proteins, *Clostridium* protein has the potential to increase exposure to nucleic acids when substituting for conventional meat or dairy products in the diet. However, this contribution is not expected to be greater than that of the existing fungal protein counterparts currently on the market.

An assessment of the mineral profile of *Clostridium* protein was conducted by comparing the estimated intakes of each element under the conditions of intended use against the Adequate Intakes (AIs) and RDAs established by the IOM (2019). Overall, *Clostridium* protein was determined to make a significant contribution to daily requirements for manganese, molybdenum and selenium but exposure is not expected to be detrimental from a nutritional or safety perspective. Likewise, analysis of the B vitamin content of *Clostridium* protein indicates that the ingredient has the potential to be a high source of vitamin B12 under the conditions of intended use but intakes will not be nutritionally disadvantageous.

Additionally, it was recognized that residual amounts of butyrate, acetate and lactate carrying over into *Clostridium* protein from the fermentation process are expected to fall well below the levels of these

organic acids and their salts used as additives in food in the U.S. Thus, no safety concerns were anticipated from the presence of low levels of these fermentation metabolites in the food ingredient.

The allergenic potential of *Clostridium* protein was evaluated by *in silico* methods using the criteria described by Codex Alimentarius Commission on foods derived from biotechnology (Codex, 2009; Goodman *et al*., 2008). The results of protein analysis support that *Clostridium* protein does not pose a realistic risk of food allergy to consumers. These findings are consistent with the low oral allergenic risk generally associated with microbial species.

Although the available evidence on the microbial source indicates it is non-pathogenic and non-toxigenic, there is insufficient body of knowledge of *Clostridia* species or products derived thereof, in food. On this basis, toxicological testing of *Clostridium* protein was warranted.

A battery of toxicity tests were conducted using *Clostridium* protein, specifically a dose-range-finding (DRF) study in rats, a 90-day dietary feeding study in rats and two *in vitro* genotoxicity assays. The methodology used for the toxicity assessment of *Clostridium* protein is consistent with the general principles laid down in the U.S. FDA Redbook Chapter III for the assessment of food ingredients. The findings of these studies are published and provide pivotal evidence of the safety of the ingredient for the intended use in conventional foods and beverages (Jonaitis *et al*., 2022).

The 90-day feeding study was conducted in male and female rats provided 0 (control), 5.0, 7.5 or 10.0% *Clostridium* protein in the diet as a partial replacement for casein. Comparable growth performance was observed among dietary treatment groups consistent with *Clostridium* protein providing a digestible and high-quality protein source for rats. Based on the results of this study demonstrating an absence of any adverse effects related to inclusion of *Clostridium* protein in the diet, the highest treatment level of 10.0%, corresponding to 5,558 and 6,671 mg/kg body weight/day for male and female rats, respectively was determined to be the NOAEL.

Under the conditions of intended use of *Clostridium* protein in conventional foods and beverages, on a body weight basis, infants and young children were determined to have the highest mean and 90$^{th}$ percentile consumer-only intakes of 600 and 1,370 mg/kg body weight/day, respectively. The amount of *Clostridium* protein fed to female rats in the 90-day dietary feeding study was 4-fold higher than the highest 90$^{th}$ percentile intakes estimated from the proposed food uses of the ingredient.

The nucleic acid content of the lot of *Clostridium* protein used in the 90-day dietary feeding study was determined analytically to be 2.7 g/100 g. Exposure to nucleic acids by rats consuming diets containing 10% *Clostridium* protein was estimated to be 149 and 179 mg/kg body weight/day in male and female rats, respectively. As mentioned above, under the conditions of intended use, infants and young children were determined to have the highest mean and 90$^{th}$ percentile consumer-only intakes of 600 and 1,370 mg/kg body weight/day, respectively of *Clostridium* protein, equating to 24 and 55 mg nucleic acids/kg body weight/day for an ingredient containing the maximum amount of 4 g nucleic acids/100 g. The amount of nucleic acids from *Clostridium* protein fed to female rats in the 90-day study was 3-fold higher than the highest 90$^{th}$ percentile intakes estimated from the proposed food uses of the ingredient.

Genotoxicity studies are not normally conducted on novel proteins, but considering the microbial source and the absence of any established history of use of *C. tyrobutyricum* or products derived thereof, as

food ingredients, evaluation of the genotoxic potential was considered pertinent to the safety evaluation. Consistent with the WGS and bioinformatics analysis, the results of the *in vitro* genotoxicity tests demonstrate that *Clostridium* protein is non-genotoxic.

It is generally recognized that the standard battery of testing in animals has limitations when applied to macronutrients on the basis that there are practical limitations in deriving NOAELs or tolerability limits. The concentration of the test item generally cannot be incorporated into the diet at sufficiently high levels to derive the conventional 100-fold safety factor allowing for intra- and inter-species variation without resulting in nutritional imbalances which can lead to secondary consequences such as adverse physiological effects (Borzelleca *et al*., 1996; Munroe *et al*., 1996; EFSA, 2011b). The findings of the 90-day dietary feeding study in rats was therefore, considered together with characterization data on the strain, the nutritional properties of the ingredient, *in vitro* digestibility data and allergenic potential, to provide a weight of evidence assessment of the safety of *Clostridium* protein under the conditions of intended use.

Following a critical evaluation of the data and information summarized above, it can be concluded that *Clostridium* protein manufactured by Superbrewed Food using suitable food-grade materials in accordance with cGMP and meeting appropriate food-grade specifications, is safe and suitable for the intended use as a source of protein in the range of specified conventional foods and beverages. It is further concluded that *Clostridium* protein is GRAS for the intended use in food based on scientific procedures.

**CONCLUSIONS**

We, the undersigned independent qualified members of the Expert Panel, have independently and collectively critically evaluated the data and information summarized above and conclude that *Clostridium* protein manufactured by Superbrewed Food in accordance with cGMP and meeting appropriate food-grade specifications as presented in the supporting dossier [Documentation to Support the Generally Recognized As Safe (GRAS) Status of *Clostridium* Protein for Use in Foods], is safe and suitable for use as an ingredient in specified food and beverage products.

We further unanimously conclude that the proposed use of *Clostridium* protein manufactured in accordance with cGMP and meeting food-grade specifications is GRAS based on scientific procedures.

It is our opinion that other qualified experts would concur with these conclusions.

[redacted]

Professor Eric Johnson
University of Wisconsin-Madison

5/15/2022
Date

[redacted]

Professor Kelly Swanson
University of Illinois, Urbana-Champaign

05/16/2022
Date

[redacted]

Dr. Ashley Roberts
AR Toxicology, Inc.

05/12/2022
Date

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE (Subpart E of Part 170)

Form Approved: OMB No. 0910-0342; Expiration Date: 07/31/2022
*(See last page for OMB Statement)*

**FDA USE ONLY**

| GRN NUMBER | DATE OF RECEIPT |
|---|---|
| 001129 | Dec 14, 2022 |
| ESTIMATED DAILY INTAKE | INTENDED USE FOR INTERNET |
| NAME FOR INTERNET | |
| KEYWORDS | |

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: 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.

## SECTION A – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*

☒ New ☐ Amendment to GRN No. _____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3 Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd):* 2022/06/29

4 For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication *(yyyy/mm/dd):* _____

## SECTION B – INFORMATION ABOUT THE NOTIFIER

**1a. Notifier**

| Name of Contact Person | Position or Title |
|---|---|
| Bryan P. Tracey | CEO |
| Organization *(if applicable)* | |
| Superbrewed Food, Inc. | |
| Mailing Address *(number and street)* | |
| 239 Lisa Drive | |

| City | State or Province | Zip Code/Postal Code | Country |
|---|---|---|---|
| New Castle | Delaware | 19720 | United States of America |

| Telephone Number | Fax Number | E-Mail Address |
|---|---|---|
| 1 (864) 921 5146 | | btracy@superbrewedfood.com |

**1b. Agent or Attorney *(if applicable)***

| Name of Contact Person | Position or Title |
|---|---|
| Elizabeth Lewis | Scientific & Regulatory Advisor |
| Organization *(if applicable)* | |
| NutraSteward Ltd. | |
| Mailing Address *(number and street)* | |
| Frederick House, Johnston | |

| City | State or Province | Zip Code/Postal Code | Country |
|---|---|---|---|
| Haverfordwest | Pembrokeshire | SA62 3AQ | United Kingdom |

| Telephone Number | Fax Number | E-Mail Address |
|---|---|---|
| 44(0)7847301171 | | elizabeth.lewis@nutrasteward.com |

## SECTION C – GENERAL ADMINISTRATIVE INFORMATION

1. Name of notified substance, using an appropriately descriptive term

Clostridium protein

2. Submission Format: *(Check appropriate box(es))*

☒ Electronic Submission Gateway

☐ Electronic files on physical media

☐ Paper

If applicable give number and type of physical media

_____

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in CFSAN's files? *(Check one)*

☐ Yes *(Proceed to Item 5)* ☒ No *(Proceed to Item 6)*

5. The submission incorporates information from a previous submission to FDA as indicated below *(Check all that apply)*

☐ a) GRAS Notice No. GRN _____

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for conclusions of GRAS status *(Check one)*

☒ Scientific procedures *(21 CFR 170.30(a) and (b))* ☐ Experience based on common use in food *(21 CFR 170.30(a) and (c))*

7. Does the submission (including information that you are incorporating) contain information that you view as trade secret or as confidential commercial or financial information? (see 21 CFR 170.225(c)(8) and 170.250(d) and (e))

☐ Yes *(Proceed to Item 8*

☒ No *(Proceed to Section D)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, information is designated at the place where it occurs in the submission

☐ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☐ No

## SECTION D – INTENDED USE

1. Describe the intended conditions of use of the notified substance, including the foods in which the substance will be used, the levels of use in such foods, and the purposes for which the substance will be used, including, when appropriate, a description of a subpopulation expected to consume the notified substance.

Clostridium protein is intended for use as a source of protein in meat and poultry analogs, dairy analogs, prepared meals, meal replacement products, milk and non-milk-based nutritional beverages, vegetable and fruit-based drinks, baked goods, breakfast cereals, soups, dressings and sauces at levels ranging from 1 to 40% by weight of the ready-to-eat (RTE) or the ready-to-drink (RTD) products. In protein powders for formulation into beverages using milk or water for consumption as a supplemental protein source in the diet, use levels will vary up to a maximum of 90% by weight in the powder.

2. Does the intended use of the notified substance include any use in product(s) subject to regulation by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture?

*(Check one)*

☐ Yes ☒ No

3. If your submission contains trade secrets, do you authorize FDA to provide this information to the Food Safety and Inspection Service of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☐ No , you ask us to exclude trade secrets from the information FDA will send to FSIS.

## SECTION E – PARTS 2 -7 OF YOUR GRAS NOTICE

*(check list to help ensure your submission is complete – PART 1 is addressed in other sections of this form)*

☒ PART 2 of a GRAS notice: Identity, method of manufacture, specifications, and physical or technical effect (170.230).

☒ PART 3 of a GRAS notice: Dietary exposure (170.235).

☒ PART 4 of a GRAS notice: Self-limiting levels of use (170.240).

☒ PART 5 of a GRAS notice: Experience based on common use in foods before 1958 (170.245).

☒ PART 6 of a GRAS notice: Narrative (170.250).

☒ PART 7 of a GRAS notice: List of supporting data and information in your GRAS notice (170.255)

**Other Information**

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☒ Yes ☐ No

Did you include this other information in the list of attachments?

☒ Yes ☐ No

## SECTION F – SIGNATURE AND CERTIFICATION STATEMENTS

1. The undersigned is informing FDA that Dr. Bryan Tracey
*(name of notifier)*

has concluded that the intended use*(s)* of Clostridium protein
*(name of notified substance)*

described on this form, as discussed in the attached notice, is (are) not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is generally recognized as safe recognized as safe under the conditions of its intended use in accordance with § 170.30.

2. Superbrewed Food, Inc. agrees to make the data and information that are the basis for the conclusion of GRAS status available to FDA if FDA asks to see them; agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so; agrees to send these data and information to FDA if FDA asks to do so.
*(name of notifier)*

239 Lisa Drive, New Castle, DE 19720
*(address of notifier or other location)*

The notifying party certifies that this GRAS notice is a complete, representative, and balanced submission that includes unfavorable, as well as favorable information, pertinent to the evaluation of the safety and GRAS status of the use of the substance.The notifying party certifies that the information provided herein is accurate and complete to the best or his/her knowledge. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

| 3. Signature of Responsible Official, Agent, or Attorney | Printed Name and Title | Date (mm/dd/yyyy) |
|---|---|---|
| Elizabeth Lewis Digitally signed by Elizabeth Lewis Date: 2022.12.14 16:01:17 -04'00' | Dr. Elizabeth Lewis, Scientific & Regulatory Advisor | 12/07/2022 |

## SECTION G – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

| Attachment Number | Attachment Name | Folder Location (select from menu) (Page Number(s) for paper Copy Only) |
|---|---|---|
| | GRAS Notice_Clostridium Protein_2022-1207.pdf | Submission |
| | RedactedbySubmitter_GRAS Notice_Clostridium Protein_2022-1207.pdf | Submission |
| | App A_Clostridium Protein_Consensus Statement_2022-1207.pdf | Submission |
| | RedactedbySubmitter_App A_Clostridium Protein_Consensus Statement_2022-1207.pdf | Submission |
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**OMB Statement:** Public reporting burden for this collection of information is estimated to average 170 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, **PRAStaff@fda.hhs.gov**. (Please do NOT return the form to this address). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.