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ORIGINAL SUBMISSION

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December 22, 2009

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Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: Proteus - GRAS Notification for Beef Protein

To Whom It May Concern:

This letter is submitted in triplicate to provide the Center for Food Safety and Applied Nutrition (CFSAN) with notice that our client, Proteus Industries, Inc. ("Proteus"), has concluded that the use of beef protein[1] in further processed (or finished) beef products is exempt from the pre-market approval requirements applicable to food additives under the Federal Food, Drug, and Cosmetic Act ("FD&C Act"), 21 U.S.C. § 301 et seq., because such use is generally recognized as safe ("GRAS"). 21 C.F.R. § 170.30.

Reference is made to prior submissions made through another law firm of March 3, 2004[2] and May 18, 2005,[3] also on behalf of Proteus. These prior notifications discussed the manufacture and usage of certain fish and poultry products derived from virtually identical technology. For the sake of efficiency CFSAN may wish to consult the prior documents.

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[1] Unless specified, "beef protein" and "protein" in this document will refer to both beef protein and concentrated beef protein.

[2] GRAS Notice No. GRN 147, dated March 3, 2004, amended March 10, 2008, for seafood protein.

[3] GRAS Notice No. GRN 168, dated May 18, 2005, for poultry protein.

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Division of
Biotechnology and
GRAS Notice Review

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Also, since the beef protein will be used in beef products, which are subject to inspection by USDA's Food Safety and Inspection Service (FSIS). We are therefore also providing a copy of this notification document to the FSIS Risk and Innovations Management Division. We would encourage your efforts to coordinate your review of this request consistent with the policies of both agencies. We will be pleased to assist in this process in any appropriate fashion.

As explained below, beef protein is acceptable for use in all further processed beef products unless such use is specifically precluded by a recipe-type standard of identity. Moreover, to assure compliance with applicable labeling requirements, the presence of any such substance should be identified, in the appropriate order of predominance, in the ingredient statement of any finished beef product. 21 C.F.R. § 101.4(a)(1). 9 C.F.R. § 317.2(c)(2).

To ensure that your agency will be able, consistent with its established policy, to properly evaluate and respond to this notice within 180 days, this notice tracks the prescribed format and provides a description of the information that the agency considers appropriate to support a GRAS determination as set forth in the Proposed rule, "Substances Generally Recognized as Safe," 62 Fed. Reg. 18937 (April 17, 1997) (proposed 21 C.F.R. § 170.36).

1. Name and Address of the Notifier (Proposed Sec. 170.36(c)(1)(i))

As indicated above, beef protein is produced by Proteus Industries, Inc., which is located at 15 Great Republic Drive, Gloucester, MA 01930. The agency should feel free to contact Dr. Stephen Kelleher at this address for further technical information regarding this notification

(Telephone: (978) 281-9545 / Facsimile: (978) 281-9542 / E-mail:

sdkelleher@proteusindustries.com).

2. Common or Usual Name of the Substance (Proposed Sec. 170.36(c)(1)(ii))

An appropriate descriptive name for the substance developed by Proteus for use in finished beef products is "beef protein" when the protein concentration is 18% protein or less, or "concentrated beef protein" when the protein concentration is greater than 18% protein.[4] Since there are no relevant standards or common or usual names for such products, Proteus' responsibility is to identify an accurate, non-misleading descriptive name. 21 C.F.R. § 101.3(b)(2)-(3). 9 C.F.R. § 317.2(c)(1). Use of the terms "beef protein" or "concentrated beef protein" performs such a function in that such terms correctly identify the food substance, which results from a process in which the protein component of beef tissue has been extracted. In addition, there is ample precedent at FDA for similar labeling of other vegetable-based protein products produced in a similar fashion. See 21 C.F.R. § 102.22.

Implicit in such a labeling decision is recognition of the fact that the citric acid (or similar food grade, incidental additive)[5] used in the initial processing is appropriately classified as a

[4] Eighteen percent (18%) is the approximate protein concentration found in beef muscle. (USDA Nutrient Database).

[5] Any food grade acid is acceptable for purposes of processing the beef protein. Although this document discusses citric acid specifically and provides levels of use and residual presence for citric acid, Proteus may in the future use other food grade acids in the product's manufacturing process, and it expects the properties and levels to be comparable.

processing aid.[6] In the proposed formulation, the citric acid fully complies with the FDA definition of a "processing aid" promulgated at 21 C.F.R. § 101.100(a)(3)(ii) in that the citric acid is added to the food for its technical or functional effect in the processing, but it is present in the finished beef product at insignificant levels and does not have a continuing technical or functional effect in that food. See 21 C.F.R. § 101.100(a)(3)(ii)(c).

As described below, the acid extracts and purifies the muscle protein and stabilizes the pH in the processing, but it is subsequently decreased during the ultrafiltration process.[7] The citric acid does not provide any additional technical or functional effect in the finished beef product. Reducing the amount of citric acid in the finished beef product further removes any sour taste. Filtration, be it ultra- or micro-, is the only method that simultaneously lowers the acid content while concentrating the protein.

3. Conditions of Use (Proposed Sec. 170.36(c)(1)(iii))

This beef protein will enhance the formulation of a wide variety of further processed beef products. Given its high protein content, it will impart considerable nutritive value to such

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[6] Citric acid is affirmed as a GRAS substance. See 21 C.F.R. § 184.1033.

[7] Citric acid as well as salt and water are reduced during the ultrafiltration process because, in contrast to the protein, the small size of the compounds relative to the membrane filter size enables their passage through the filter to the permeate or effluent stream. For example, if we have 100 ml and the starting protein concentration is 21.0 mg/ml and starting citric acid concentration is 2 mg/ml, then we have 2100 mg protein and 200 mg citric acid. Initially, the citric to protein ratio is 200/2100 = 0.10. If we concentrate one time then the protein content stays at 2100 mg (protein does not go through the filter) and the citric acid content becomes 100 mg for a ratio of 100/2100 = 0.048. Therefore, we have removed the citric acid from the isolated, concentrated proteins.

products. In addition, it will have binding characteristics and, as such, might be used in lieu of chemical agents such as phosphates and/or other binding ingredients.

The foods to which the resulting protein can be added are all beef products that have musculature. Furthermore, while the protein can be added to any beef muscle, economics dictate that it would be most feasible for higher value products.

Beef protein is added to muscle in beef products because the protein has been found to reduce volume shrinkage and increase moistness in the final cooked product while maintaining a high protein level in the finished product. The level used in the final product varies depending upon the final concentration of protein in the protein solution. The higher the protein concentration, the greater the amount that can be applied to the musculature because the solution will contain less water. A detailed analysis of the method of monitoring protein concentration during the ultrafiltration process is provided below in Section 6.

One level of use may be a 10% application rate of an 8% protein solution. A common edible portion of beef would be 4 oz (112 g) raw beef which cooks to 3 oz (84 g). The resultant cooked portion would have 0.03 oz (0.90 g) of added protein and 0.001 oz (0.022 g) of citric acid. In "Average Annual Per Capita Consumption of Meat" (National Cattleman's Beef Association, 2009), it was stated that the per capita consumption of edible beef muscle in the US was 62.7 lbs per year in 2008. Using this figure, it would translate to an average consumer ingesting approximately 8.1 oz (225.7 g) of added protein and 0.2 oz (5.51 g) of citric acid per year.

The population expected to consume the protein would be any persons who eat beef. The protein could be injected or mixed into beef portions directed for both fresh and frozen markets. Both fresh and frozen beef with incorporated beef protein could be used without additional processing or further processed into value-added products, such as sausage, hamburger, pizza toppings, frankfurters, battered alone, or battered and breaded, such as in country fried steak. The protein solution could also be used as a coating, spraying the protein onto a breaded substrate prior to deep fat frying. By using the protein from the identical species, the consumer would be able to avoid any potential allergen issues.

4. Basis for the GRAS Determination (Proposed Sec. 170.36(c)(1)(iv))

As explained below in Section 8, the basis for the GRAS determination is "through scientific procedures."

5. Availability of Data and Information (Proposed Sec. 170.36(c)(1)(v))

The data and information that are the basis for the GRAS determination are available for CFSAN's review and copying at reasonable times at 15 Great Republic Drive, Gloucester, MA 01930 or, upon request, can be sent to CFSAN for review.

Very truly yours,

(b) (6)

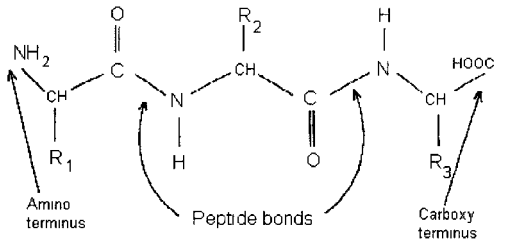
Robert G. Hibbert

cc: Proteus Industries, Inc.

A. Identity and Specifications of Beef Protein or Concentrated Beef Protein (Proposed Sec. 170.36(c)(2))

Proteins play an essential role in human nutrition and are utilized by food manufacturers for their functional properties, such as gelatin, water binding ability, fat binding ability, thickeners/viscosity builders, and foaming agents. All proteins follow the same building block format where amino acids are linked together through peptide bonds (**Figure 1**). The linking together of different amino acids in varying sequences is what determines the final structure of the protein and explains why proteins, which basically follow the same construction format, can be totally different in primary, secondary, tertiary, or quaternary structures.

Figure 1. ***Basic Primary Protein Structure***



The protein profiles of beef protein extracted from beef using acid solubilization are very similar. **Figure 2** (following page) shows the results from an SDS-PAGE separation of proteins from beef muscle used as the starting material for the protein extraction process. (The SDS-PAGE photographs are done in duplicate and one should focus on lanes 1, 4 & 5 for beef.)

Figure 2. ***SDS-PAGE (4-20% linear gradient) of pork and beef muscle at selected steps in the protein solubilization process.***

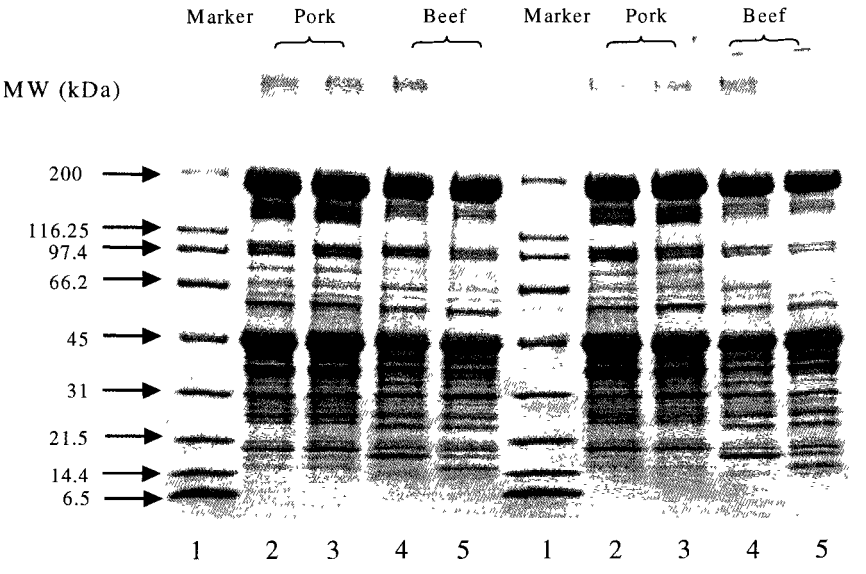


Figure 2 Protein profile of pork chop and beef paste at selected steps in the protein solubilization process. Lane 1: molecular weight marker; lane 2: pork chop muscle; lane 3: pork chop protein sediment at pH 5.5; lane 4: beef paste; lane 5: beef paste protein sediment at pH 5.5; fractionalized by SDS-PAGE (4-20% polyacryamide gels). Protein was applied to all lanes at 17μg/lane except molecular marker.

An examination and comparison of lanes 4 and 5 for beef in **Figure 2** evidences the strong similarity in protein profiles of both muscle (beef paste) and protein (beef paste protein sediment) extracted from like source muscle using acid solubilization.

The protein is extracted using a mild technique which relies on adjustment of pH and salt conditions that perturbs the protein slightly to unfold and expose previously buried hydrophobic areas of the protein. (Kelleher 2000, Kelleher *et al.* 2003). Under low ionic conditions, these

unfolded proteins interact to a greater extent with the surrounding water, thus becoming soluble and allowing the removal of insoluble impurities, which is the purpose of the process.

The concentrated beef protein will be manufactured by Proteus in cooperation with its customers at various facilities using the following procedures. (For a pictorial view of the manufacturing processes, we refer you to **Figures 3, 4** (following pages).

The starting material will be in the form of mince or trimmings in either fresh or frozen form. The starting material of choice will be 50/50 (lean/fat) trimmings. The starting muscle source could originate from any edible muscle source including, but not limited to, trim from chuck, or loin.

During the initial processing stage, the starting material will be mixed with cold, potable water to form a slurry. Citric acid (or similar food-grade, acidulant product) will be used for the specific purpose of extracting and purifying the muscle protein and stabilizing the pH of the solution. This is the full extent of the technical or functional effect of the acid. At this point in the manufacturing process, we would estimate, on a percentage basis, that the mixture in question would be comprised of approximately 20 percent meat tissue, 79.6 percent water, and 0.4 percent citric acid.

The next step in the process is for these materials to be centrifuged (if the material contains a high content of lipid) or filtered in order to remove or reduce fat and other incidental constituents and materials including contaminants, such as residual bone or skin material, impurities, flavors, odorous compounds, and cholesterol. The remaining mixture would consist of protein, water, and acid with very low amounts of remaining lipid. After the centrifuge or

filtering processes are completed, we anticipate that the resulting material would consist of approximately 1.9 percent protein, 97.7 percent water, and 0.4 percent acid.

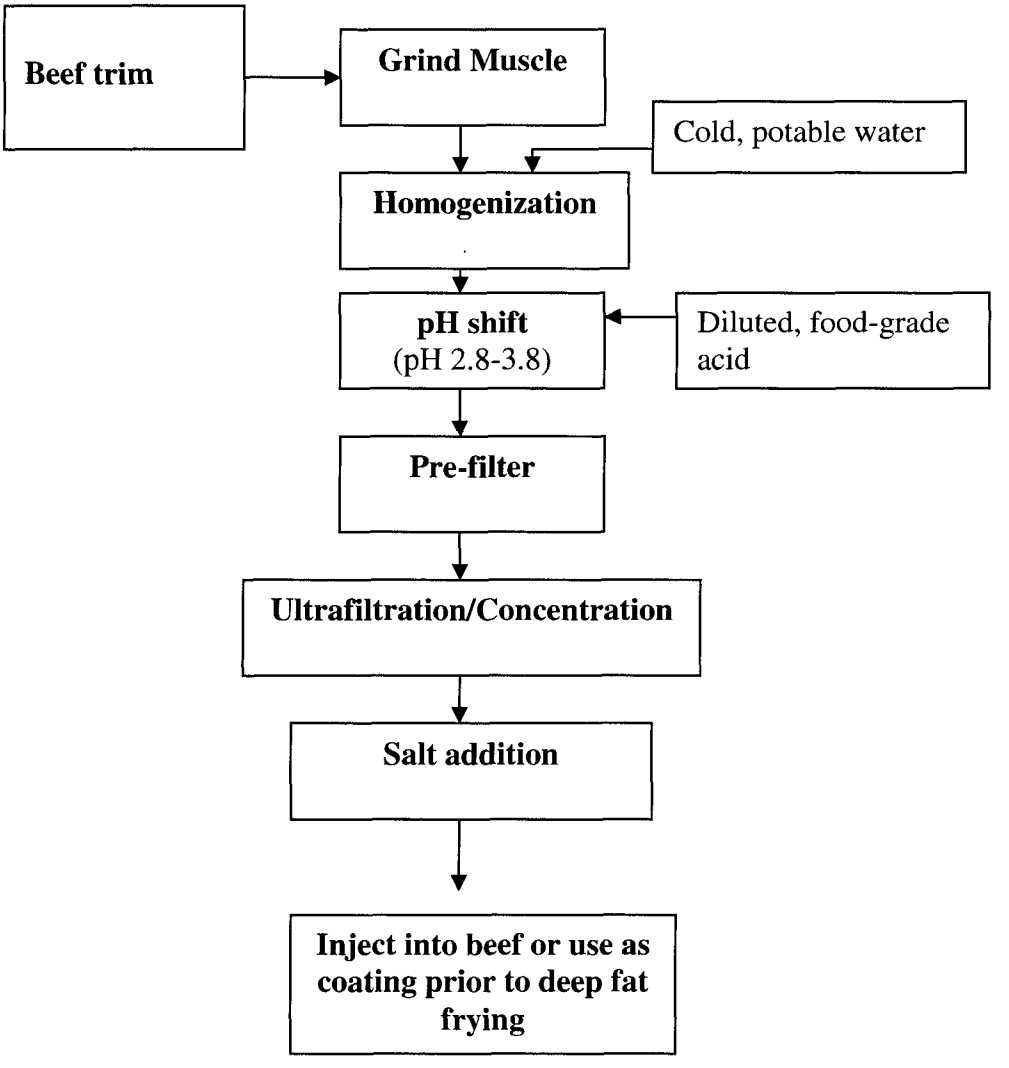


Figure 3. ***Steps in the acid solubilization protein extraction process.***

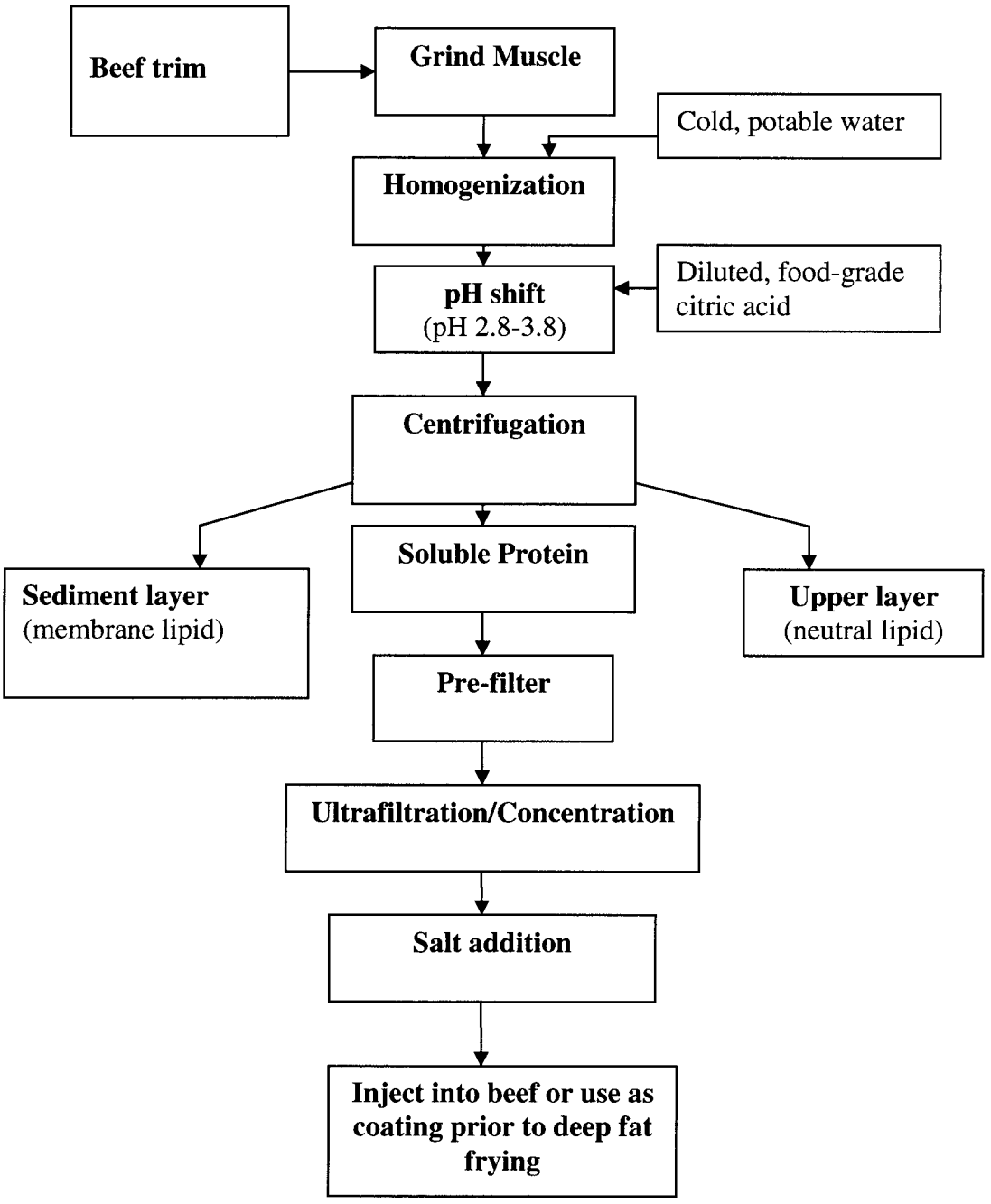


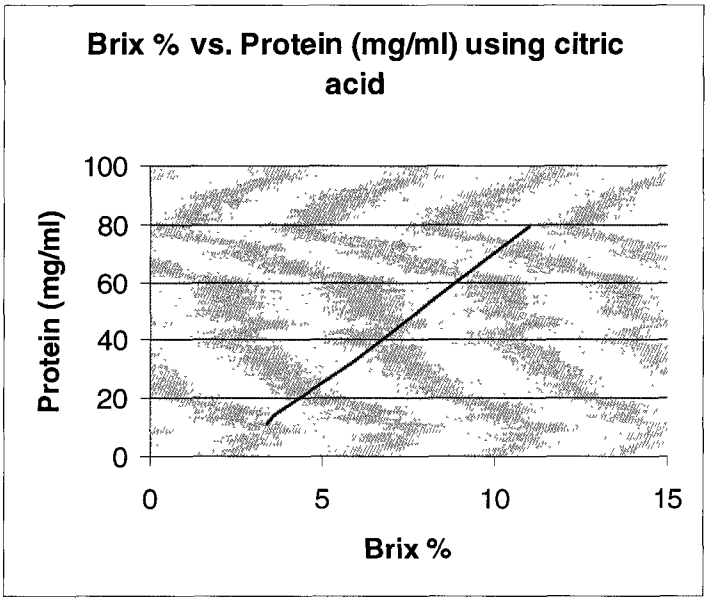
Figure 4. ***Steps in the acid solubilization protein extraction process with centrifugation steps.***

The next step is to subject the material in question to an ultrafiltration process. The net effect of ultrafiltration is to remove a significant amount of the product's moisture, as well as reduce the acid, which was added for the sole technical or functional purpose of extracting and purifying the muscle protein and stabilizing the pH during the earlier processing stage. The acid can be reduced by a factor of two to seven times during the ultrafiltration process. By lowering the citric acid while concentrating the protein, the citric acid to protein ration decreases as ultrafiltration proceeds. The ultrafiltration process also removes salt. The resulting thin-syrup like product is expected to have a protein content between 2-12% and a moisture content range between 88-98%.

Proteus monitors the protein concentration during the ultrafiltration process by utilizing a refractometer which measures soluble solutes (protein being soluble) on a Brix % scale. As the solution concentrates, the Brix % increases. Standard curves (**Figure 5**; following page) relating Brix % to protein concentration can be plotted.

The test was set up to take aliquots of protein solution during different stages of concentration. The protein content is measured, using the Biuret Method (Torten and Whitaker, 1969) and the Brix %. Plotting the two produces a straight line, which enables Proteus to track the protein using the very simple Brix% test (Brix requires about 1 second to run, whereas protein can take about 1 hour).

Figure 5. Standard curve for Brix% versus protein concentration.[8]



Proteus may modify this ultrafiltration process to obtain some variability in the protein content of any finished substance. Using large pore, hollow fiber, ultrafiltration columns, the amount of salt is reduced by an approximate factor equal to the reduction in volume. This results in a salt to protein ratio in the dewatered protein solution that can be lower than in the original tissue. Salt can be added back to the protein solution at a level not to exceed the original tissue salt level. Returning the tissue to the original protein to salt ratio has been shown to improve functionality of the proteins compared to the reduced salt proteins.

The next step is to incorporate the recovered proteins back into tissue of identical species of similar origin. The proteins are added back to the tissue using injection, mixing, static soaking, vacuum tumbling, or as a coating. If the proteins are delivered into or on finished

[8] Gornall, AG, CS Bardawill, and MM David. *J. Biol. Chem. 177:* 751. 1949.

product tissue at 5 and 10% application rates, then the acid level in the final tissue would maximally be between 0.02 and 0.04%, respectively.

The substance is very digestible and is characterized by a fast absorption rate. The extracted proteins have amino acid contents similar to beef flesh, including high levels of aspartic acid, glutamic acid, and lysine (**Figure 6**). The percentage essential amino acids from the starting beef was 42.81%, whereas for the acid solubilized beef protein it was 46.31%. This suggests that little destruction or crosslinking occurred to the amino acids during the protein extraction process.

Figure 6. ***Amino acid profile of beef muscle and protein extracted from the same beef muscle using acid solubilization, processed according to US Patent 6,005,073***

Amino acid	*Protein from Beef (% of total protein)*	*Acid solubilized protein from same Beef (% of total protein)*
Aspartic acid	10.65	11.07
Threonine*	4.39	4.51
Serine	5.59	6.15
Glutamic acid	16.25	16.39
Glycine	7.72	4.51
Alanine	6.72	5.74
Valine*	4.46	4.51
Methionine*	2.86	2.46
Isoleucine*	3.79	3.69
Leucine*	8.39	8.20
Tyrosine	3.20	3.28
Phenylalanine*	4.73	4.10
Lysine*	10.79	12.30
Histidine*	3.40	6.56
Arginine	7.06	6.56

* essential amino acids (not including tryptophan)

Figure 7 illustrates the effect of the protein extraction process on some endogenous, muscle, tissue components.

Figure 7. ***Moisture, protein, lipid and phospholipid contents in beef and acid solubilized beef protein***

Beef Sample	Moisture (%)	Protein (%)	Lipids (%)	Phospholipids (mg/100g)
Raw Beef	65.76 ± 0.32	19.87± 0.96	14.82± 0.38	369.63 ± 77.30
Acid solubilized Beef Protein	76.77 ± 0.21	21.51 ± 0.91	2.19 ± 0.03	532.91 ± 71.74

Values are means ± standard deviation on a wet weight basis. Protein was determined using the Biuret method as described by Torten and Whitaker (1969). Lipid was determined using a 1:1 chloroform:methanol extraction solution as described by Lee *et al* (1996). Phospholipid was estimated as phosphorus determined by the dry ashing method of Kovacs (1986) and the assumption that the average MV of phophotidylcholine was 750 daltons.

Through the process there was a 100% recovery of the proteins, 85% reduction in total lipid and a 44% increase in phospholipids in beef protein. Phospholipid increase may be explained due to the fact that the process preferentially removes neutral lipid leaving the phospholipids associated with the cellular membranes intact.

Removal of the lipid components can reduce the concentration of lipid soluble components. Proteus has been issued a patent (US Patent # 7,033,636) on the reduction of cholesterol when using the soluble proteins in combination with ultrafiltration as described above. Metals, such as iron, are more soluble in oil than in water. Removal or reduction of lipid, hence also the metal components, appears to increase the stability of the final extracted proteins, possibly due to reduced iron (Fe^{+2}) being a known catalyst for oxidation and lipid oxidation reactions as described in the Fenton Equation.

$Fe^{+2} + H_2O_2 \rightarrow Fe^{+3} + OH^{-} + HO^{\cdot}$ ($HO^{\cdot}$ is the reactive compound)

The extracted proteins have also been evaporated to an 18% total solids syrup and spray dried to a stable powder that both can be stored without losing their functionality.

Proteus is unaware of any potential human toxicants associated with the extracted proteins.

B. Self-Limiting Levels of Use (Proposed Sec. 170.36(c)(3))

Proteus has found that injecting the beef protein at percentages greater than approximately 18% (w/w; at pH 3.2 using citric acid) may result in a sour taste in the injected products.

C. Scientific Procedures GRAS Determination (Proposed Sec. 170.36(c)(4))

Proteus has determined that the beef protein discussed in this GRAS notification is exempt from premarket approval because such use is GRAS as determined through scientific procedures. That is, there is reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. Moreover, the information supporting this expert consensus is generally available.

The use of acid solubilized proteins from fish and mammalian muscle tissue, while a relatively new concept, has been covered in much detail in the food scientific literature. Most covered in the literature is the use of acid solubilized proteins for the manufacture of surimi, a crab or seafood analog product. However, there are also papers covering beef and chicken.

The safe recovery and use in foods of acid solubilized proteins has been described in the peer reviewed literature by Hultin and Kelleher (1999), Kelleher and Hultin (1999), Hultin and Kelleher (2000), Kelleher (2000), Kelleher and Hultin (2000), Hultin and Kelleher (2001), Cortes-Ruiz *et al.* (2001), Choi and Park (2002), James *et al.* (2003), James and Mireles DeWitt (2002), Mireles DeWitt *et al.* (2002), Undeland *et al.* (2002), Kim *et al.* (2003), Undeland *et al.* (2003), and Kelleher *et al.* (2003). Numerous presentations have also been given on the acceptability of acid solubilized proteins as potential foods, such as those at the Institute of Food Technologists (IFT) Annual Meetings, Pacific Fisheries Technologists (PFT) Annual Meetings, More Efficient Utilization of Fish and Fisheries Products Conference (MEUFFP), Kyoto, Japan, October 2001, and recently at the Trans Atlantic Fisheries Technology (TAFT) Conference held in Reykjavik, Iceland, June 2003.

In these papers and presentations are statements referring to the acid isolated proteins as nutritious, healthful, and a responsible use of by-product proteins for human food use. In Section 3, this document described the probable portion intake of the isolated proteins (0.90 g) and citric acid (0.022 g), a value which is quite low when compared against the US RDA of proteins at 63 g protein and the amount of citric acid typically found in orange juice (1%). Proteus is unaware of any potential substances being formed in or on muscle foods due to incorporating acid solubilized, isolated proteins into them.

Proteus also does not believe that there is any cumulative effect of its isolated proteins in a diet. Both citric acid and isolated proteins have a high degree of water solubility, which makes them less susceptible to accumulation in humans as would lipid soluble ingredients. Proteus has

been monitoring research in the field of acid soluble proteins since approximately 1996 and is not aware of any reports of investigations or other information that would be inconsistent with a beef protein GRAS determination.

Storing or treating muscle proteins in acid as a food has historically been done in the preparation of products such as pickled herring. The acid that appears in most formulas is acetic acid (vinegar). Fish muscle is placed in a solution of acid and salt and marinated for long periods of time after retorted in bottles or cans. Proteus has been unable to find references to the ill effects of consuming acidified, pickled fish products. Proteins of all muscle groups also come in contact with stomach acids as part of the digestion process, and this is believed to be a step in improving the nutritional bioavailability of the proteins.

A Canadian company that has been testing the use of low pH extracted proteins with Proteus has been advised by Health Canada to follow their labeling requirements that require that any protein isolate have a mandatory common name of and be labeled "the name of the source of the protein plus protein" or "the common name of the protein isolate". Following these rules using beef, FDRB.01.010(3)(a) (Annex, 1, Part 7), "beef protein" would be appropriate.

There are presently many research groups throughout the United States and the world examining the use of acid solubilized proteins as a food. These research groups are looking at the process for extracting proteins from fish or animals local to them, thereby expanding the regional knowledge.

The use of proteins as a food has been the topic of seminars and demonstrations given at Oregon State University Surimi School (1999-2002), where Dr. Michael Morrissey (Oregon

State University), Dr. Jae Park (Oregon State University), and Dr. Stephen Kelleher (University of Massachusetts) led and participated in discussions on the use of acid solubilized proteins as food. "The use of small pelagics for food applications through the recovery of functional proteins and fish oils" (Dr. Michael Morrissey, Principal Investigator) was a project, funded by Oregon SeaGrantin in March 2004.

There has been other funded research on acid solubilized proteins for use as foods. There was a three-year ($1.3 million USD) Nordic Industry Fund Grant to researchers in Sweden, Iceland, Denmark, and Norway who studied the isolated proteins from herring by-product in frozen and dried form to be used as seafood analogs, emulsifying agents, and water and fat binding agents. The project manager was Ms. Margret Giersdottir, Icelandic Fisheries Laboratory, in Reykjavik, Iceland. Dr. Christina Mireles DeWitt (Oklahoma State University) also has researched extracting acid solubilized proteins from beef muscle by-product and catfish frames, both funded by the state of Oklahoma. Dr. Mireles DeWitt has been funded and published in the past on extracting proteins from beef hearts using the low pH extraction process. Dr. Jae Park recently presented a paper at the American Meat Science Association, Reciprocal Meat Conference (Park, 2009) where he summarized and documented much of the research that is being performed world-wide on acid solubilized proteins. Proteus also has commercial experience using "fish protein" and "chicken protein" made in a similar fashion to the proposed "beef protein", involving approximately 10 million lbs. of finished product coated using like species proteins for schools (Child Nutrition - CN), food service, quick service restaurants, and the military. That figure is highly expected to grow to 40-50 million lbs./year in 2010.

It is Proteus' belief through discussions with the above mentioned experienced and widely regarded food science researchers that there is a consensus that the beef protein that is the subject of this GRAS notification is generally recognized as safe for addition to human food.

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SUBMISSION END

From: Murphy, Grace H.
To: Mcmahon, Carrie;
cc: "Robert.Ragland@fsis.usda.gov"; Hibbert, Robert G.; Fasano, Jeremiah;
Subject: Proteus letter - supplemental information for GRN 313 and 314
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Dear Dr. McMahon,

Please find attached a letter with responses to FDA's questions on the separate GRAS notifications for Beef and Pork protein. Please let us know if there are additional questions.

Separately, we are finalizing the suitability petitions for the beef and pork proteins and should have them submitted to FSIS before the end of the week. We will certainly copy you when we submit those files.

Best,

Grace

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Re: Proteus – Supplemental Information for GRAS Notifications for Beef (GRN 313) and Pork (GRN 314) Protein

Dear Dr. Fasano:

This letter responds to FDA's questions regarding the GRAS notifications, originally submitted December 14, 2009 and revised December 22, 2009, for Beef protein (GRN 313) and Pork protein (GRN 314) in which our client, Proteus Industries, Inc. ("Proteus"), concluded that the use of beef protein in further processed (or finished) beef products and the use of pork protein in further processed (or finished) pork products are exempt from the pre-market approval requirements applicable to food additives under the Federal Food, Drug, and Cosmetic Act ("FD&C Act"), 21 U.S.C. § 301 et seq., because such use is generally recognized as safe ("GRAS"). 21 C.F.R. § 170.30.

We respond to each of FDA's questions:

1. FDA Question: What steps has Proteus taken to ensure that bovine spongiform encephalopathy (BSE) is not an issue with respect to beef protein? More specifically, what steps in the manufacturing process are designed to ensure that nervous tissue and other tissues potentially capable of transmitting BSE are not present in the trimmings and mince used as the source material for beef protein?

Response: In response to the public health concern regarding BSE, FSIS issued a series of three interim final rules[1] on Jan. 12, 2004. These rules prohibit human consumption non-ambulatory

[1] 69 Fed. Reg. 1862, 1874, and 1885 (January 12, 2004).

"downer" cattle and cattle tissue identified as specified risk materials (SRMs); banned the use of high pressure stunning devices that could drive SRM tissue into the meat; and established requirements for Advanced Meat Recovery systems. See 9 C.F.R. §§ 309.2, 309.3, 310.22, 311.27, 318.6(b), 319.5(b), 318.24, 320.1(b)(10), 313.15

In addition, FSIS policy gives a clear definition of meat (9 C.F.R. §§ 301.2 and 318.24) that does not include brain, trigeminal ganglia, spinal cord tissue, or dorsal root ganglia, all of which are central nervous system-type tissues. Therefore, product containing spinal cord tissue is not allowed to be called meat.

In a Fact Sheet on its website, FSIS also states:

> **Will FSIS test product produced by AMR systems for spinal cord tissue and dorsal root ganglia?**
>
> Yes. In March 2003, FSIS began a routine regulatory sampling program to ensure that plants using AMR systems are preventing spinal cord from entering the food supply in products labeled as meat. The sampling program will be expanded to also test for the presence of dorsal root ganglia, and will include meat from beef and pork.
>
> **What actions will FSIS take if spinal cord or dorsal root ganglia are found in product produced by AMR systems?**
>
> Establishments must ensure that bones going in to the AMR system do not contain fragments of brain, trigeminal ganglia, or spinal cord. In addition, the product exiting the system cannot have spinal cord or dorsal root ganglia. If FSIS observes any bones entering the AMR system with these central nervous system-type tissues, the product that is produced will not be allowed to be labeled as meat. In addition, if tests on the product exiting the AMR system identify the presence of spinal cord or dorsal root ganglia, inspection personnel will withhold marks of inspection from the establishment's AMR product and tag the AMR system itself, meaning neither the product nor the equipment can be used until satisfactory corrective action has been taken. If the establishment has distributed the sampled product then the product will be subject to recall. Inspection personnel conduct follow-up sampling to verify that the establishment has taken appropriate corrective action. AMR production will not be allowed to resume until FSIS determines that corrective actions have been successful.
>
> **How will FSIS ensure that these SRMs are not present in human food?**
>
> Slaughter and processing establishments will be required to develop procedures to show that SRMs are removed from product. To ensure that SRMs are not present

> in meat, FSIS inspectors will verify that establishments are properly removing these tissues. In addition, FSIS will continue a strong regulatory verification testing program of product produced from AMR systems to ensure that spinal cord and dorsal root ganglia are not present in meat.
>
> Also, because vertebral column and the skull of cattle older than 30 months will be considered inedible, these materials cannot be used in AMR systems.

See FSIS Further Strengthens Protections Against Bovine Spongiform Encephalopathy (BSE), *available at* http://www.fsis.usda.gov/Fact_Sheets/FSIS_Further_Strengthens_Protections_Against_BSE/index.asp.

Proteus obtains its beef and pork as frozen material with USDA inspection marks from USDA-inspected facilities. Since Proteus is not involved with the slaughter or recovery of meat from the animals, Proteus relies on the FSIS inspectors and their certifications that the beef and pork are suitable for use in human food. Proteus has built into its HACCP plan that it will only use approved suppliers that conform to all USDA regulations.

2. FDA Question: Proteus states in both GRN 000313 and 000314 that the ingredient's use is self-limiting because use levels above 18% produce a sour taste. Given that the process described in these notices produces an end product with variable concentrations of both citric acid and protein, we would appreciate a more complete and precise description of the product's self-limiting properties (e.g., by defining a minimal protein/acid ratio, and relating that to a maximal use level).

Response: The upper limits of the use for beef and poultry were originally based on the poultry precedent, which was set at 18% protein in solution. To be more specific, Proteus has updated the maximum use level to reflect the actual "protein" limits.

The upper limit of beef and pork protein that is used to block fat and retain moisture when delivered as a solution is as follows:

- when applied as a protein coating only, not to exceed 0.8% by weight of the final product formulation
- when used in the batter only, not to exceed 0.14% by weight of the final product formulation, and
- when used as both a coating and in the batter, not to exceed 0.89 % by weight of the final product formulation

When used in a marinade, the beef or pork protein is not to exceed 0.8% by weight of the final product formulation.

3. FDA Question: Is the application rate 5%-10% based weight of raw pork product at time of formulation/application?

Response: Yes, the application rate is based on the weight of the raw pork product at the time of formulation/application. However, as the 5-10% application rate was given as an example use, please note there may be other uses beyond that range.

FDA Question: FDA and USDA request that you clarify the intended use of beef protein and pork protein, as described in GRAS notices GRN 313 and GRN 314, respectively. In your notices, you refer to "further processed (or finished) beef products" and "further processed (or finished) pork products."

Response: Proteus intends, as a condition of use, that the beef or pork products containing the respective beef or pork protein will be further processed before they are sold to the consumer (e.g., beef or pork protein will be used in products that are sold at retail as cooked ready-to-eat beef sausages, hot dogs, etc.). Proteus also intends that the "beef protein" will be marketed at retail in raw beef products such as beef patties, cut of meat steaks and roast that do not receive further processing. Similarly, the "pork protein" will be marketed at retail in raw pork products that do not receive further processing.

Please do not hesitate to contact me if you have additional questions.

Sincerely,

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Robert G. Hibbert

cc: Carrie McMahon, Ph.D., CFSAN, Division of Biotechnology and GRAS Notice Review
Robert D. Ragland, DVM, MPH, FSIS, Risk & Innovations Management Division